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EDITED BY GEORGE MORRIS PIERSOL, M.D.

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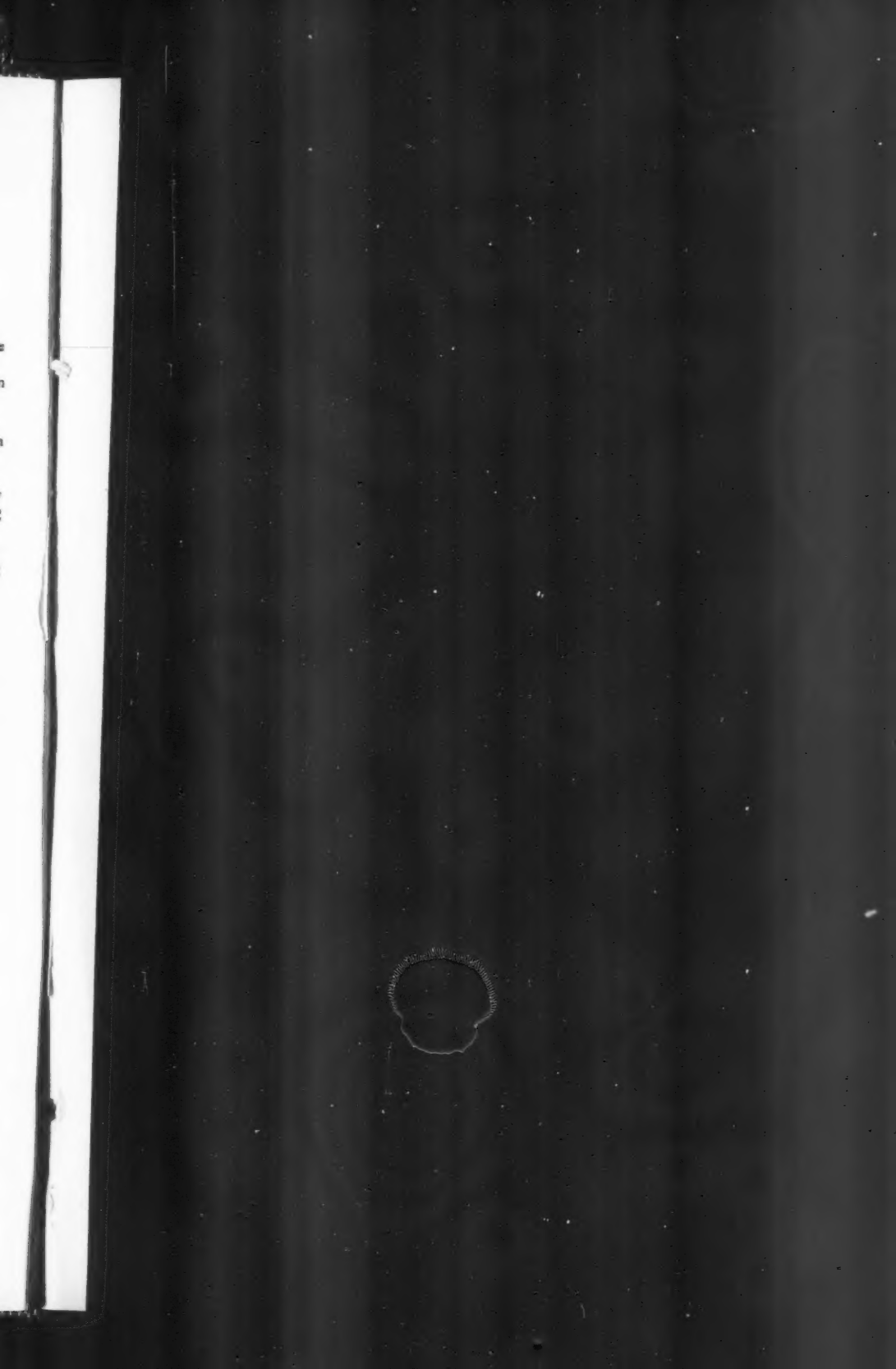

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THE SPECIFICITY, DANGER, AND ACCURACY OF THE TUBERCULIN TESTS.[1]

By Lawrason Brown, M.D.,

ADIRONDACK COTTAGE SANITARIUM, SARANAC LAKE, N. Y.

During the past ten years a great change of opinion has taken place in regard to the tuberculin test. The subcutaneous test with its disagreeable reaction has deterred many from using tuberculin diagnostically, and not until von Pirquet described his cutaneous modification and Wolff-Eisner and Calmette their conjunctival test, has tuberculin been universally used. These and other modifications have greatly extended our knowledge of this subject and it has seemed fitting at this time to review briefly my experience with tuberculin used for diagnosis and to draw whatever conclusion about its value that seem warranted.

1. The Specificity of Tuberculin. However it may be with diseases not transmissible to the ordinary laboratory animals, certainly among these animals only those react to the tuberculin tests which are tuberculous. Tuberculin, as Citron and others have shown, is not an ordinary toxin. Normal animals have tuberculin tolerance but no tuberculin anaphylaxis; tuberculous animals have tuberculin anaphylaxis and acquire tuberculin tolerance when properly treated with tuberculin. Normal animals may acquire anaphylaxis after injection of tuberculin when the second dose is

[1] Read before the Association of American Physicians, May 9–10, 1911.

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1. The Specificity of Tuberculin. However it may be with diseases not transmissible to the ordinary laboratory animals, certainly among these animals only those react to the tuberculin tests which are tuberculous. Tuberculin, as Citron and others have shown, is not an ordinary toxin. Normal animals have tuberculin tolerance but no tuberculin anaphylaxis; tuberculous animals have tuberculin anaphylaxis and acquire tuberculin tolerance when properly treated with tuberculin. Normal animals may acquire anaphylaxis after injection of tuberculin when the second dose is

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given intravenously or intracerebrally, but Baldwin and Krause have been unable to produce any sensitiveness to tuberculin in normal guinea-pigs when the second dose is given cutaneously, intracutaneously, subcutaneously, or in the conjunctiva. This suggests that some difference exists between the mechanism involved in the ordinary tuberculin test and that concerned in anaphylaxis, though the difference is probably one only of degree. In Koch's first paper he called attention to the fact that it required 250 mg. to make him react, and in 1891 and again last year, reports have been published showing that infants, apparently healthy, fail to react to very large doses, even 1000 mg. repeatedly given. This simply bears out the experimental fact that only animals infected with tubercle bacilli react.

Many autopsy reports throw grave doubt upon, and personally, I believe, disprove all published statistics which go to show that other diseases (particularly syphilis) react specificially to tuberculin, but indicate that they are in reality instances of double infection. The cutaneous test has shown that patients with these diseases react to tuberculin in about the same proportion as ordinary individuals in poor health. That a slight tuberculous infection may be sufficient to cause reaction for a time and yet leave no permanent pathological change visible to the naked eye, is readily possible.

Leprosy, however, must be considered separately, for the interesting work of Babes suggests that while most of the lepers who react to tuberculin are tuberculous as well, still it is impossible in some to find any evidence of it clinically or at autopsy, and the reddening of the leprous nodules three days after the injection of tuberculin is of considerable interest. The reaction, he believes, is specific for leprosy in that it begins later (twenty-four hours) and lasts longer (for several days) than in the tuberculous, possibly not reaching its maximum until the third or fourth day. The cutaneous test is often absent, while in 50 per cent. of Babes' cases the conjunctival test was positive. Leprosy and tuberculosis are rarely confused, and the presence of lepra bacilli in numbers in the nasal discharge is of great aid in differentiation.

Recent work has tended to show that sensitiveness to the tuberculin tests cannot be produced in healthy individuals. This does away with any fear of a too slow increment of dosage and permits one to use and to draw diagnostic conclusions from a clinical course of tuberculin treatment. A slight reaction to a small dose at any time during the course of treatment would be proof sufficient that the patient had had a tuberculous infection.

2. The Danger of Tuberculin.—The conjunctival test has produced a number of unfortunate accidents, one of which, a central corneal opacity, came under my observation after the administration of the test dose. When the subcutaneous test follows a

positive conjunctival test, the eye may react again, or even during tuberculin treatment there may be for a time slight reddening. These objections, with the exception of the injury to sight, are of small moment and when carefully given, excluding all patients who have ever had the slightest trouble with their eyes and using only 1 and 5 per cent. solutions of the old tuberculin, the test seems comparatively safe. General reactions have followed its use, and on the whole it should be avoided in children.

The cutaneous test has produced lymphangitis, extending from the forearm to the elbow or even the shoulder, with slight swelling of the lymphatic glands in several instances, and in another case rather extensive ecchymosis but no necrosis. Several general reactions have occurred in my patients. Certainly the dangers of the cutaneous test are so slight as to warrant no consideration except in scrofulous children.

The subcutaneous test to be positive demands a general reaction, and anyone who has experienced a severe reaction to tuberculin will agree with me that the ordeal is, to say the least, decidedly unpleasant. In the majority of patients the only symptom remaining at the end of the second or third day is a little weakness, which is speedily replaced in many instances by a feeling of improvement. I have repeatedly been asked on this account by these patients for permission to take tuberculin therapeutically. On the other hand, in a few instances, I have seen a slight temperature persist for months after a subcutaneous test when it had been normal previously. In one case expectoration, which had been absent before, was present for two or three years afterward, but it is no uncommon thing for patients who have never had tuberculin to present similar histories. In several instances, on the other hand, patients to whom we were about to administer tuberculin, but for some reason failed to do so, had attacks of pleurisy, hemiplegia, etc.

The discovery for the first time of tubercle bacilli in the sputum just after a subcutaneous tuberculin test, often only indicates that the sputum had not been examined frequently enough before the test. Without doubt tubercle bacilli are present in the sputum of many patients when, after one or two ordinary examinations, they are stated to be absent. In one instance we gave 0.2 and 1 mg. to a patient with negative sputum without reaction of any sort and then found tubercle bacilli in the sputum, which had again become slightly blood-streaked. In another apparently doubtful case, while we were considering the use of the tuberculin test, we found tubercle bacilli in the sputum.

The occurrence of tubercle bacilli in the sputum following or after this test has long been held as proof of the lytic activity which many assume to occur during this reaction. In the 286 tests under

consideration, tubercle bacilli were found in the sputum subsequent to the test in 18, fourteen times in the incipient and four in the moderately advanced cases. In order to connect the test with the occurrence of tubercle bacilli as cause and effect, we must establish some limit of time in which the tubercle bacilli must occur. I have arbitrarily chosen two months, but in most instances all effects of the reaction have passed in two or three days. Of these 18 cases, 5 incipient and 2 moderately advanced occurred within this period, 4 within one and 3 within two months. In one instance included here, the test was negative, in another tubercle bacilli were found before a single subcutaneous dose was given while in a third the test was given while the patient was waiting admittance and before the sputum was subjected to as prolonged search as afterward. If we exclude these 3, the figures would indicate that tubercle bacilli are two or three times as likely to occur after as within the time limit of two months. When it is considered that tubercle bacilli occurred after the test in only 6 per cent. of 286 cases, and that in less than 2 per cent. did there occur bacilli within two months after the test, it seems that little weight can be attached to the tuberculin test as the cause of the occurrence of tubercle bacilli in the sputum. If the occurrence of tubercle bacilli in the sputum after the subcutaneous test was connected with the test it is only reasonable to expect to find some signs of congestion and softening in patients whose sputum later showed the presence of tubercle bacilli. In only 2 of the 18 cases previously mentioned were the respiratory symptoms increased, 1 of which was the instance where there was only an intradermic test. In all, 40 patients showed some increase of the respiratory symptoms, and in only 1 could the reaction be considered in any way connected with the occurrence of tubercle bacilli in the sputum. My experience, therefore, leads me to believe that any apparent connection is due entirely to coincidence.

At the Adirondack Cottage Sanitarium, our routine has been to require all patients who have never had tubercle bacilli in their sputum to undergo the subcutaneous test. More recently I have come to hesitate about giving it. When a patient is doing well it is a curious thing that very little seems required to upset the balance and turn, for a time at least, the scale against him. The greatest danger that I have seen result from the subcutaneous test is such a slight temporary disturbance; but without doubt, more danger, however slight, is connected with this test than with the cutaneous or intradermic tests.

3. The Focal Reaction in the Lungs. An increase of physical signs occurred in the lungs in 39 per cent. of 127 patients who were carefully examined, during the reaction and for the most part two days later, or if we include 17 doubtful cases in 45 per cent.

The occurrence of this so-called focal reaction seems to be little connected with the severity of the reaction as manifested either by the symptoms or by the degree of temperature. Symptoms referable to the respiratory tract seem to occur with about equal frequency in those with and in those without increase of physical signs. These respiratory symptoms, however, were in almost every case connected with marked general symptoms, but apparently occurred independently of the degree of fever and showed very little tendency to occur more frequently in early stages of the disease. In a few cases the increased physical signs, persisted, and it is possible that in these and in a few others they were overlooked at the first examination.

4. The Value of the Tuberculin Test. A test, to be of real value, should enable us to differentiate not only tuberculosis from other diseases, but also clinical tuberculosis from non-clinical tuberculosis. The latter I define as an infection with tubercle bacilli, which has not reached a stage in which it can be diagnosticated clinically, while the definition of "clinical tuberculosis" is self-evident. Clinical tuberculosis may be masked, active, quiescent, or arrested, stages which can be separated only by the symptoms and physical signs which the patient presents, or by the lack of them.

The occurrence of a tuberculin reaction in apparently healthy men is an interesting phenomenon which would occur probably in a large percentage of middle-aged individuals. It varies, as Franz has shown, more or less directly with the incidence of tuberculosis in the race. It possesses in health no clinical importance, If, however, these same healthy men later fall ill of non-tuberculous diseases, what is going to prevent their reacting, in part at least, to tuberculin? Nägeli's figures and Franz's statistics both warn us of the danger of depending too much upon this test.

In my experience at the Adirondack Cottage Sanitarium, where for several years all patients without tubercle bacilli in the sputum have been required to undergo the subcutaneous test as a routine measure, I have come to believe that failure to react to 10 mg. of old tuberculin, given subcutaneously, does not exclude clinical tuberculosis. However, in the presence of indefinite symptoms, it indicates that in all probability, treatment is unnecessary. I have allowed these patients to return home at once, and so far no doubtful clinical case, which has failed to react to 10 mg. has relapsed, after one to six years, though we have had only 12 such cases. Nine other cases reacted first to 10 mg. One patient who failed to react to 6 mg. was classified as doubtful for several years, but finally relapsed, had tubercle bacilli in his sputum, and tuberculous cervical glands.

I have no doubt that some patients who react to doses much

smaller than 10 mg. may suffer only from tuberculous infection, and that the symptoms they present may be due to causes other than tuberculosis. Over one-half (52 per cent.) of our advanced cases reacted to 1 mg. or less, while considerably less than half of the incipient cases (42 per cent.) reacted to the same dose. In only 4 per cent. of the advanced and 15 per cent. of the incipient cases was it necessary to give over 5 mg. to produce reaction. A negative subcutaneous test in a tuberculous patient may indicate either the absence of receptors at the site of the lesion or the presence of free antibodies in the blood. In a certain number of these cases complement deviating substances (amboceptors) have been found in the blood, and in the patient whose clinical history and physical signs point strongly to a diagnosis of tuberculosis, the occurrence of these substances may explain the negative subcutaneous test.

Healthy infants do not react to 1000 mg. Some patients with clinical tuberculosis react only to 10 or more milligrams. There is, therefore, no known limit at which a healthy man will react and no known limit which divides patients with tuberculous infection from those with clinical tuberculosis. Certainly, failure to react to 10 mg. or less does not surely disprove the presence of clinical tuberculosis. Of 9 patients, who failed to react to 10 mg. given subcutaneously, 4 reacted to the cutaneous test, while 3 failed to do so to old tuberculin in full strength, and 2 showed a positive local reaction (Stickreaktion). One of the 3 patients with a negative cutaneous reaction reacted to the intradermic test. The local reaction was positive in every instance (176) where it was noted in patients who reacted to the subcutaneous test.

The cutaneous test is of value in early life, though when its reliability ceases is difficult to determine. Certainly, after seven or eight years, a positive reaction is of little value, for by this time tuberculous infection and clinical tuberculosis are vastly different things, and without doubt the great majority of both react to the cutaneous test. I cannot yet accept a negative skin reaction as excluding either tuberculous infection or clinical tuberculosis, as I know of tuberculous patients in good condition who have failed to react to old tuberculin in full strength. This absence of reaction of the skin or conjunctiva may indicate only that no sessile receptors are present in these parts, not that the patient is without tuberculous infection. Many attempts have been made by graduating the dose in the cutaneous test, to separate clinical tuberculosis from tuberculous infection. Ellerman and Erlandsen believe that they have accomplished this, and suggest the use of a rather complicated formula based upon the differences of the average diameters of the papules when four scarifications have been made through four simultaneously applied doses of tuberculin, each four times stronger than the preceding, for example, 0.5 per cent., 2 per cent., 8 per

cent. and 32 per cent. O. T. Some have not been able to verify the work of Ellerman and Erlandsen, nor has it been proved, providing a sufficient amount be used, that the quantity of the solutions plays a very important part. My experience leads me to believe that the more nearly the technique approaches that used for vaccinia, the more reliable the results. In any individual patient, if he react to one drop of 1 per cent. or of a 5 per cent. solution of old tuberculin given in different eyes, he is more likely to have clinical tuberculosis than if he reacted only to the cutaneous test.

The intradermic test should, theoretically, be far more accurate than either the conjunctival or the cutaneous test, however applied, for all the tuberculin given reaches the interior of the skin. It admits further of accurate dosage which, on account of the possible variation in power of absorption of the skin and the difficulty of keeping all the solution over the abrasion or in the conjunctiva until absorbed, is impossible in either the cutaneous or the conjunctival tests. In some instances certainly it is more sensitive than the skin test, reacting where the latter is absent. While a dose of 0.02 of a milligram has never caused a general reaction, we have no record of any patient failing to react to this dose given intradermically.

In brief, if we except for the time being, leprosy, tuberculin is a specific test for the detection of tuberculous infection. The danger from the use of the tuberculin test is slight, but in some unsuitable cases very real and possibly severe. Reaction, even when severe, has no connection with the appearance of tubercle bacilli in the sputum. Increase of physical signs occurs in about one-third of all the cases and in one-half of those with increase of pulmonary symptoms and is independent of the appearance of tubercle bacilli in the sputum. In practice, exposure to infection, characteristic symptoms, such as hemoptysis, pleurisy with effusion, dry pleurisy on both sides, and localized persistent physical signs at one apex, are diagnostic data of far more importance in clinical tuberculosis than that derived from the tuberculin tests. A positive reaction, when only doubtful symptoms of pulmonary tuberculosis are present, is of uncertain value unless the pulmonary symptoms or signs are definitely increased during the reaction. A negative reaction is of uncertain value, and in the face of positive symptoms carries little weight. In many instances the tuberculin tests add only confusion to the clinical data. The subcutaneous test, depending as it does upon the reaction at the site of the lesion, is still today the most reliable of the tuberculin tests; but neither this nor any of the modifications as yet devised, differentiate clearly clinical tuberculosis that demands vigorous treatment from non-clinical tuberculosis that requires only a God-fearing life.

TUBERCULOUS INFECTIONS CLASSIFIED FOR AID IN DIAGNOSIS AND TREATMENT.

A. Diagnosis.

I. Non-clinical tuberculosis.
No symptoms or physical signs.
May or may not react to tuberculin tests.
II. Clinical tuberculosis.
With symptoms or physical signs or both.
Usually react to tuberculin tests.
(*a*) Masked.
Physical signs only, no symptoms.
(*b*) Active.
Symptoms present.
Physical signs usually present.
(*c*) Quiescent or arrested.
Symptoms present now or formerly.
Physical signs present or absent.

B. Treatment.

A. Not necessary.
I. Non-clinical tuberculosis.
II. Clinical tuberculosis.
(*a*) Masked.
B. Necessary now or formerly.
II. Clinical tuberculosis.
(*b*) Active.
(*c*) Quiescent or arrested.

IS PERNICIOUS ANEMIA OF INFECTIOUS ORIGIN?[1]

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SINCE Addison's description, various types of anemia due to carcinoma, sepsis, parasites, etc., have been differentiated, but there is still left a large group of cases for which the title of cryptogenetic pernicious anemia must be preserved. No matter where

[1] Read before the Association of American Physicians, May 10, 1911.

seen—in Austria, Switzerland, Germany, Paris, London, Boston, or California—these cases are symptomatically remarkably alike. The difficulties of distinguishing the characteristic blood changes from so-called secondary anemias seem to me much exaggerated. Clinically, the general appearance of the patient, the fever, the cardiovascular, gastro-intestinal, and nervous symptoms, the peculiar remissions, pathologically the pronounced fatty degenerations, the siderosis in liver, spleen, and kidneys, the marrow changes, are as characteristic of the disease as the blood picture. The constancy of these phenomena in practically all cases is in favor of a definite clinical entity, the result of some specific intoxication.

Nearly all authors now agree that the marrow changes are secondary, represent regenerative efforts, and are not in any way specific. Recent investigations have been concerned chiefly with causes of the pathological hemolysis, which is a main feature of the disease. Experimentally by injection of toluylendiamine, ricin, pyridin, saponin, hemolysis may readily be induced and marrow changes and a blood picture may result that closely resemble those of pernicious anemia. Schaumann, Faust, and Tallquist have shown that the anemia due to bothriocephalus is the result of hemolysis produced by a lipoid substance that may be extracted from the segments. In these cases, also, lipoid bodies are to be found in increased amounts in the gastro-intestinal tract. The hemolytic substance isolated by Tallquist was either the sodium or cholesterin combination with oleic acid; normally but little cholesterin was to be found in blood, and when a certain concentration was reached hemolysis occurred. Tallquist suggested therapeutically calcium salts or glycerin to form insoluble or harmless compounds with oleic acid. On the other hand, von Eisler, following the observation of Kruskal that serum inhibited to a certain degree the hemolytic action of saponin, showed that this was due to cholesterin, and Ransome demonstrated that the specific resistance of the erythrocytes was likewise dependent upon cholesterin. In animals, the resistance to saponin hemolysis runs parallel with the cholesterin content of the serum. Morgenroth and Reicher, working with cobra venom and other toxic lecithins, proposed the use of cholesterin therapeutically to inhibit hemolysis. Fejes has recently written of anemia produced experimentally by bacterial hemolysins. Berger and Tsachiya extracted a lipoid substance from the intestinal mucous membrane of individuals dying from pernicious anemia, and found its hemolytic action ten times more potent than extracts from other cases. Anemia of the pernicious type resulted from its injection in animals, a similar lipoid could be obtained from the gastro-intestinal mucous membrane of dogs after production of moderate inflammatory changes. Schlaepfer, employing the method of Ciaccio for preserving lipoids, found lipoid bodies in the intestinal mucous membrane of two cases of pernicious anemia;

in a normal intestine and in a case of secondary anemia they were not obtained. The reports about the various lipoids are, however, still conflicting; other observers have extracted hemolytic substances from the normal intestine, so that we must conclude that no specific toxic body has yet been found.

The recent paper of Grawitz advocates anew the theory of gastro-intestinal intoxication and lays particular stress upon the absence of hydrochloric acid in the stomach as an important factor. But achylia may exist for years without anemia, it is associated not infrequently with intestinal parasites—tenia, uncinariasis, amebiasis—and may result from malignant disease in any part of the body. It is a symptom and not a cause of pernicious anemia. The writer has seen several cases treated by the Grawitz method progress steadily to a fatal issue. Witherspoon has reported a number of cases apparently benefited by measures directed toward the gastro-intestinal tract. In one instance, the symptoms and the character of the stools were influenced favorably by appendicostomy and irrigation. Favorable results have followed the administration of lactic acid preparations. Grawitz would interdict animal albumin in the diet, while Strauss and others advocate overfeeding with meat and peptones. The absence in the majority of cases of signs of intestinal putrefaction, the remarkable appetite and digestion exhibited by many patients, the improvement and apparent cure that may occur without any treatment whatsoever, the persistence of the achylia during remissions—these fact are decidedly against a primary gastro-intestinal intoxication as a cause of the disease. The crises of vomiting and diarrhea not infrequently observed resemble closely the attacks in the course of exophthalmic goitre. Improvement of all symptoms and of the blood picture may follow such a crisis and suggests the elimination of toxic products or the destruction of great numbers of parasites.

Comparatively little has been done in searching for an infectious cause of pernicious anemia. Swiss authors have dwelt upon the occasional endemic occurrence. In the past year, I have seen 7 cases from one of the large interior valleys of California, 3 being from a town of 10,000 inhabitants. Rarely the disease has been observed in two or more members of a family. Of interest in connection with the pernicious anemia of horses, later to be described, is the opinion of some foreign authors that the affection is more commonly met with in country districts. Of 25 cases seen by the author in the past two years, only ten were in city dwellers. The statistics of Cabot, however, by far the best at our command, show that place of residence and condition of life have no influence in etiology.

The theory of buccal or gastro-intestinal infection advanced by Hunter, has been generally abandoned—the sore mouth, not infrequently seen is a symptom and not a cause of the disease. Von

Jacksch, and more recently G. Klemperer have suggested a protozoal origin. Hoefer in a case with recurring fever once, during a period of temperature, observed some peculiar bodies both within and outside the red corpuscles. They resembled piroplasma, but were larger; culture and animal experiments were negative.

Many points of similarity between trypanosomiasis or piroplasmosis and pernicious anemia suggest the possibility of a protozoal infection.

1. Anemia is a prominent feature in many forms of trypanosomiasis and in piroplasmosis—in surra, dourine, caderas, galziekte. In kala azar anemia is usually moderate, but Sheka and Zoypfl have reported the case of a boy, aged nine years, with a count of 2,400,000 red and 1100 to 2000 white cells. In infantile splenic anemia, the result of infection with Leishmania infantum, very low counts have been recorded. In Texas fever in cattle when organisms appear in the peripheral blood, sixty to eighty days after the infecting tick bite, anemia gradually becomes apparent, anisocytosis, poikilocytosis, polychromatophilia, basophilia occur, and normoblasts and megaloblasts later appear. Leukopenia, relative lymphocytosis, and a high color index usually are feature of these protozoal infections.

2. Fever occurs in 79 per cent. of the cases of pernicious anemia (Cabot). Its frequency speaks against a purely toxic cause. It may continue for weeks, may recur periodically, or may be absent during long remissions. Similar peculiarities of the temperature are observed in trypanosomiasis. In certain instances of pernicious anemia, high temperature, profound exhaustion, marked nervous symptoms, and a considerably enlarged spleen speak strongly in favor of a rapidly progressing infection.

3. The remissions of pernicious anemia are among the most remarkable features of the disease; similar remissions are characteristic of a number of protozoal infections. The recurrence of all clinical phenomena of the disease and progression to a fatal issue after remissions of five, ten, fifteen, and even twenty years, make one hesitate to speak of cures in pernicious anemia. Todd, in a recent paper, has emphasized the long periods of apparent freedom in human and animal trypanosomiasis, five and eight years before a final relapse proves fatal.

4. The nervous symptoms and lesions of pernicious anemia, syphilis, and trypanosomiasis are, as Mott and other have pointed out, decidedly similar. But little work has yet been done on the cerebrospinal fluid in cases of pernicious anemia with cord symptoms. In two cases I have found a moderate increase of small mononuclear cells and a positive Nonne, but no Noguchi reaction.

These cases, as well as two others without spinal fluid examinations gave a negative Wassermann.

5. From recent investigations, certain lipoid substances seem to play a role in hemolysis in pernicious anemia. Lipoid bodies are likewise increased in syphilis, a spirillosis, and in trypanosomiasis.

6. The only remedies of any value in pernicious anemia are arsenic and arsenical combinations, and arsenical compounds have been found a specific in syphilis and in some forms of trypanosomiasis.

The affection known as equine pernicious or infectious anemia has, of late years, been thoroughly investigated by Carré and Vallée in France, and by Ostertag, in Germany. The first-named authors succeeded in transmitting the disease by inoculation of blood intravenously and subcutaneously and by feeding blood and urine of infected animals. They found the virus potent even after passage through bacterial filters. It is questionable whether the American swamp fever is the same disease. Four years ago, cases of pernicious anemia were noted among horses in one of the interior valleys of Washington, and I am indebted to W. B. Mack, of the University of Nevada, for published reports and recent accounts of cases occurring in eastern Nevada. For fifteen or twenty years, fatalities have been noted among the horses in certain districts, and in 1906 and 1907 the disease became epidemic, causing the death of all horses on some of the ranches. Since 1907, there have been scattered cases. All ages and conditions have been attacked, the disease running an acute, subacute, and chronic course. Few animals recover, though there may be long remissions and apparent cure. The symptoms of subacute and chronic cases are very similar to those of pernicious anemia in man. Irregular high temperatures may persist for weeks or months. Progressive weakness and anemia, throbbing of the vessels of the neck, cardiac insufficiency, dyspnea, edema, paralysis of the hind extremities are the chief symptoms. The appetite is usually ravenous; enlargement of the lymphatic glands may occur. The normal blood count of horses at the altitudes involved in Nevada, about 6000 feet, is given by Mack as considerably over 8,000,000. The lowest count recorded was 2,120,000, with 7300 leukocytes and 38 per cent. hemoglobin. There is always a leukopenia in uncomplicated cases with a relative lymphocytosis—the color index is high. Macrocytosis and nucleated red cells have been observed, but Mack comments upon the fact that the changes in the erythrocytes are not as great as would be expected from the degree of anemia. The disease may be characterized by remissions exactly similar to those that occur in pernicious anemia in man.

Autopsies on fatal cases have shown extensive subserous hemorrhages, fluid in the serous cavities, spleens sometimes normal in size and again considerably enlarged. Extensive megaloblastic metaplasia of the bone marrow has been a constant feature. In two instances, in 1907, Mack succeeded in transmitting the disease to

other horses by subcutaneous injection of defibrinated blood from diseased animals. The clinical symptoms, remissions, and autopsy findings were the same as in other cases. His recent experiments have been less positive, and he writes under date of April 19, 1911: "I have been unable to find any microörganism associated with the disease which can be regarded as the causal factor. I have searched diligently for such an organism; bacteria frequently occur in the tissues, but they do not cause the disease; piroplasma or other protozoa have not been found. Some investigators consider the cause a filterable virus, but I have not demonstrated that in my cases; in fact, my inoculations have yielded somewhat conflicting and puzzling results."

During the last year several of my cases have been investigated with the idea of a protozoal origin in mind. Films have been stained or preparations made after the method of Martin and Leboef,[2] centrifugalizing 5 c.c. of blood from a vein to which 1 c.c. of 20 per cent. sodium citrate in normal salt solution has been added. Cultures have been attempted both in normal salt solution recommended by Nuttall and in the 2 per cent. citrate of sodium solution of Rogers, and on the medium advocated by Novy. No bodies resembling protozoa have been found. Inoculations in guinea-pigs have been made, using 2 to 3 c.c. of blood, with negative result. Very few inoculation experiments have been reported in human pernicious anemia. I have in mind in future inoculations of large amounts of blood, of blood from splenic puncture, and of extracts of the tissue at autopsy into dogs, monkeys, and horses. The cases most likely to give positive results are those rather rare ones marked by a rapid progressive course, high temperature, and a greatly enlarged spleen.

THE COAGULATION TIME OF THE BLOOD IN VARIOUS DISEASES.[1]

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The method of estimating the coagulation time of the blood, as described by one of us (R. D. R.) last spring before the Association

[2] Diagnostic microscopique de la trypanosomiase humaine, Ann. de l'Inst. Pasteur, 25 Juni, 1908, I, xxii, No. 6, pp. 118 to 540.

[1] Read by title before the Association of American Physicians, May 10, 1911.

of American Physicians, has been considerably used during the past winter in the wards of the Toronto General Hospital and to a less extent in the Sick Children's Hospital here. The routine work was carried out almost entirely by one of us (C. E. C. C.).

The instrument employed has proved to be a convenient one clinically, being both portable and easily manipulated.

As was pointed out when the method was first described, the results obtained by this or by any other apparatus are in no way absolute, but merely denote the coagulation time of a given blood, *in vitro*, at a given temperature. At 20° C., the temperature at which all the work was done, the average clotting time in health is about seven minutes; but the time may vary considerably from the average in normal people, just as do pulses, blood pressures, etc.

The firmness of the clot may be gauged roughly at the time of the test, but of course, cannot be expressed in figures, as the clotting time may be. This firmness of the coagulum is a very important matter, and upon it probably depends the stopping of a hemorrhage as much as it does upon the mere fact of clotting having occurred.

The results here given are too few to be of any great value, but some interesting points have come out, and moreover, as others are working with the same apparatus, in time, sufficient data may be collected to give the range of clotting in different conditions. Some 300 tests were made of the blood of about 150 patients, with the results shown in the accompanying table.

REMARKS. *Secondary Anemias.* Secondary anemias other than those due directly to hemorrhage, appeared to have a normal clotting time. Twelve observations were made upon 6 patients, with an average clotting time of 7.8 minutes, and a range of from 10.5 to 6.4 minutes. When the anemia resulted from hemorrhage, the clotting time was invariably shortened, except in the case of hemophilia, when hemorrhage appeared to have no such effect. In 8 cases of hemorrhage, with 14 observations, the average clotting time was 6.6 minutes, with a range of from 5.2 to 10 minutes. The one that showed a time of 10 minutes was a case of epistaxis in an old woman. It was not severe, but was very persistent and hard to control. There was no history in the family of bleeding nor of previous hemorrhages. In 1 case of severe traumatic hemorrhage the clotting time was 6.4 minutes. The patient was then transfused by Crile's direct method, and afterward the clotting time was practically the same (6.5 minutes). The donor, his brother, showed before the transfusion a clotting time of 8.5 minutes, and directly after one of 5.8 minutes.

Antitoxin. Some 6 healthy children were tested before and after the administration of a prophylactic dose of antitoxin. The dose given was always 500 units, which bulks about 3 c.c. There was no change produced in the clotting time.

Disease.	Number of patients.	Number of observations.	Average clotting time in minutes.	Maximum clotting time in minutes.	Minimum clotting time in minutes.	Remarks.
Acromegaly	1	5	9.4	10.4	9.0	
Addison's disease	1	4	9.3	9.7	8.9	
Anemia: (*a*) Secondary:						
(1) Not due to hemorrhage	6	12	7.8	10.5	6.4	See remarks.
(2) Due to hemorrhage	8	14	6.6	10.0	5.2	See remarks.
(*b*) Pernicious	4	8	6.7	7.4	5.2	
Aneurysm	1	5	9.4	10.7	7.0	
Antitoxin to healthy people	6	12	....	....	....	See remarks.
Appendicular abscess	1	2	9.0			
Arteriosclerosis	1	2	7.4	7.6	7.0	
Chlorosis	2	4	6.9	8.0	6.2	
Chorea	1	1	7.7			
Dermatitis exfoliata	1	2	6.5	7.0	6.0	
Diabetes insipidus	1	2	11.5	12.2	11.2	
Diabetes mellitus	3	6	7.0	8.0	5.6	
Goitre, exophthalmic	4	9	7.5	8.5	6.2	
Goitre, simple	1	2	7.2	7.2	7.2	
Eczema seborrhoicum	1	2	6.6	6.8	6.4	
Empyema	1	2	6.5	6.6	6.4	
Erysipelas	3	5	9.2	10.8	6.5	
Gastric neurosis	2	4	8.1	8.5	7.5	
Gastric ulcer	3	6	6.8	7.7	6.2	
Hemophilia	2	10	14.25	20.0	9.5	See remarks.
Heart-block	1	3	7.1	7.6	6.7	
Influenza	1	1	7.7			
Jaundice	6	10	9.6	12.0	6.5	See remarks.
Leukemia, splenomyelogenous	1	5	8.1	9.5	6.2	See remarks.
Meningitis (pneumococcic)	1	2	4.6	5.2	4.0	
Nephritis (chronic)	3	6	8.2	10.1	8.1	
Neurasthenia	1	1	7.7			
Polycythemia	1	3	10.1	10.7	9.5	
Purpura	3	8	6.2	7.6	4.9	See remarks.
Raynaud's disease	1	2	6.6	6.8	6.5	
Renal colic	1	2	8.2	8.5	8.0	
Rheumatic fever	15	38	10.2	14.3	7.0	See remarks.
Rheumatoid arthritis	1	2	6.8	7.0	6.6	
Pneumonia, broncho-	1	4	9.9	10.5	9.2	
Pneumonia, lobar	17	47	8.1	12.7	5.5	See remarks.
Septicemia	4	8	8.3	9.7	7.4	
Tuberculosis, various forms	9	18	8.9	10.4	7.0	
Typhoid fever	26	60	7.1	12.0	5.0	See remarks.
Urticaria	1	2	8.1	8.5	7.7	

Hemophilia. Two cases, both typical as regards the family tendency to hemorrhage, etc., showed very different readings as regards their time of coagulation—one giving an average of 9.5 minutes and the other one of 19 minutes. The one that showed the greater delay was given calcium lactate freely for two days, 30 grains every four hours, with a sequence of a clotting time of 20 minutes. A few days later he was given 15 c.c. of rabbit blood serum

subcutaneously without any perceptible effect upon the clotting time.

Jaundice. Six cases of jaundice showed an average clotting time of 9.6 minutes as a result of ten observations. The minimum time was 6.5 and the maximum 12 minutes. In none of them had there been any recent hemorrhage.

Splenomyelogenous Leukemia. A case of this disease, which remarkably improved as regards the blood picture under the biweekly use of *x*-rays, showed the following clotting times in relation to the white cell count: When the leukocytes were 300,000 the clotting time was 6.2 minutes; when the leukocytes were 130,000 the clotting time was 8.6 minutes; when the leukocytes were 12,000 the clotting time was 7.6 minutes; when the leukocytes were 2000 (*x*-rays stopped) the clotting time was 9.5 minutes; when the leukocytes were 2200 the clotting time was 8.5 minutes. Thus, the clotting time here showed some lengthening as the leukocytes dropped in number.

Lobar Pneumonia. Forty-seven observations were made upon 17 cases of this disease, and the average clotting time was 8.1 minutes, but ranged from 5.5. to 12.75 minutes. The clotting time did not vary with the acuteness of the infection, 2 fatal cases showing a time of 8.25 and 8.75 respectively shortly before death. No marked daily variations occurred, but 1 case that was followed daily showed a tendency to hastening of the coagulation time until the crisis, when it swung back to normal. Thus, on the fourth day the clotting time was 8.75; on the fifth day, 8.5; on the sixth day, 8.2; on the seventh day, 7.5; on the eighth day (critical), 6; on the ninth day, 7.3, and on the tenth day, 7.6 minutes.

Purpura. Three cases of this condition, in which subcutaneous hemorrhages occurred without definite cause, showed an average coagulation time of 6.16 minutes from eight observations, the range being from 4.9 to 7 minutes. Thus the clotting time in these cases seems to be rather hastened than otherwise.

Acute Rheumatism. Thirty-eight observations were made upon the blood of 15 cases of this disease, and the average clotting time was found to be 10.2 minutes, with a range of from 7 to 14.3 minutes. Thus, the clotting time in acute rheumatism seems to be lengthened. It was noted that the clotting was delayed as long as the acute pain lasted, but it did not seem to have any special relation to the degree of fever present. All these patients were freely treated with salicylates, but the delay in the clotting time was not due to this medication, as in several of the cases the first estimates were before the remedy was commenced, and in most of them the drug was still being given after the pains had ceased and the coagulation time had consequently become faster. Thus, in one of the cases the coagulation time was 14.3 minutes before any medicine had been given, and when the pain had disappeared, the time had shortened to

eight minutes, and yet the salicylates had not been discontinued. In two of the cases calcium lactate was given in 30 grain doses every four hours for two days without the clotting time being at all shortened. One case was complicated with pericarditis and another with quinsy, without any apparent effect upon the coagulation time.

Typhoid Fever. Sixty observations were made upon 26 cases of this disease, and the average clotting time was found to be 7.1 minutes, with a range of from 5 to 12 minutes. Two cases, which had phlebitis, and had been treated for four and seven days respectively, with large doses of citric acid (30 grains every four hours), showed a coagulation time of 5.3 and 7.1 minutes; 1 case showed a shortening in the clotting time of from 7.5 to 6.25 minutes following three days of profuse diarrhea. The severity of the invasion did not seem to have any effect upon the clotting time.

CONCLUSIONS. 1. The instrument used is a convenient one for clinical purposes, and gives, with constant technique, fairly constant results. Thus, if the coagulation time of an individual be estimated several times within a few minutes of each other the readings will seldom differ by more than a minute, and are usually within half that time of one another.

2. Coagulation time, as estimated *in vitro*, and a tendency to hemorrhage are not necessarily related to each other. Thus, a patient may have a fast clotting time and yet bleed freely from a slight lesion anywhere, the trouble being probably rather of vascular than of hemic origin.

3. The firmness of the coagulum is an important matter, and can be roughly gauged by this method, although the results cannot be given in figures.

4. Anemia due to hemorrhage is constantly associated with a hastened coagulation time.

5. Acute rheumatism is usually accompanied by a delay in the clotting.

6. The free exhibition of calcium lactate and of citric acid by the mouth in various diseased conditions seems to have no appreciable effect upon the coagulation time of the blood as estimated by this method.

THE PHYSIOLOGY AND PATHOLOGY OF FEVER.[1]

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OF all the symptoms which appear during the various pathological conditions of the human organism, fever, because of its frequency,

[1] Read before the Eastern Medical Society, New York.

occupies the first place. It is quite natural, therefore, that from days immemorial, it attracted the attention of physicians, who tried to explain it and the other disturbances that are connected with it. The subject presents interest not only from its practical point of view, but more so from its theoretical, because it is only after a thorough and clear understanding of the exact causes of fever that proper therapeutic measures may be applied. A great many clinicians and scientists studied these problems from their respective views, and the literature of the subject became burdened with facts. The clinician gathered information from the bed side; he watched the behavior of his patient under the influence of different infectious processes; studied them, and finally learned to recognize them from the character of the symptoms. The scientists attacked the problem from the other side. They produced the disease in animals experimentally by injecting different toxins, or produced one of the many symptoms of fever, and studied their influences on the organism.

In this brief review we will endeavor to present the most important facts and theories that have been accepted in the past few years. The first question that confronts an investigator is: What is the cause of fever?

THE CAUSE OF FEVER. Clinicians know from experience, that fever is always closely allied to infection, and that its intensity bears a direct relationship to the appearance of a new crop of micro-organisms in the blood. The temperature of the malarial patient always rises after sporulation of the plasmodium. Lüdke also found that immediately preceding the rise in temperature, microörganisms are present in the blood of patients suffering with pneumonia and typhoid fever, although their blood was sterile the previous day. These facts at once suggested that the bacteria are responsible for the disturbances.

It was at first thought that the bacteria themselves by virtue of their presence, acted like foreign bodies, and produced irritation of the respiratory, circulatory, and heat regulating centres. In fact, it was demonstrated that the injection of a fine suspension of lycopodium or starch in the blood stream of animals produced a slight rise in temperature. But, it was soon seen that this theory did not work out in all cases We meet with a great many fevers where the infection is only local, and the disturbances are general. We meet with fever in cases of fractures, subcutaneous hemorrhages and resorption of blood, where there is no accompanying infection at all. These facts compelled investigations along entirely different lines.

Billroth[2] and Weber[3] injected the products of decomposed animal and vegetable substances into the blood stream of animals, and obtained the typical symptoms of fever, with circulatory, respiratory

[1] Langenbeck's Arch., 1862, ii, 335. [2] Berlin. klin. Woch., 1864, p. 39

and nervous disturbances. The injection of substances derived from the protoplasm of non-pathogenic germs produced similar results. Lüdke showed that an animal's own tissues ingrafted into itself, as well as foreign tissues, when absorbed, caused a rise in temperature. It was further shown that the injection of sterilized and filtered bacterial culture was followed by symptoms of intoxication. All these experiments show very clearly and definitely that although the bacteria themselves, by their presence in the tissues, may act as irritants, yet in the production of fever the presence of the toxin, produced by the bacteria, and the presence of substances of albuminous nature (Krehl), produced by the dissolution of the bacterial protoplasm or body cells are of far greater importance. These substances may contain more than one toxin, each having its own specific action. It was shown that the bouillon culture of tetanus bacilli contain in addition to the tetanus producing substances, a toxin which acts on the blood (hemotoxin). From the staphylococci we can isolate a substance leukocydin which has specific toxic influences on the leukocytes. In snake venom, we can isolate a neurotoxin, which acts on the nervous system, a hemolytic substance, hemorrhagin which acts on the endothelium of the bloodvessels, and thrombase which influences the fibrin.

Similar to some of the cells of the animal body, which possess a great many functions and produce a great many ferments, so the cells of bacteria have the power of producing a great many different substances which act injuriously on the human body. Although all have not yet been isolated and the specificity of each has not yet been determined, still it is hoped that they will be in the near future. We must not assume that all bacteria produce the different toxins in the same proportions, nor that all bacteria produce the same toxins. From the fact that the infections with different bacteria produce different reactions on the part of the leukocytes, immunity and formation of antibodies, we may safely conclude that the different species of bacteria contain and produce different toxins.

Regulation of Body Temperature. The normal temperature of the body is maintained at a level, fluctuating between 36.5° to 37.5° C. It reaches its highest point at about 7 P.M., and its lowest point at about 6 A.M. Under normal conditions it seldom passes these limits. The most important factors which are responsible for the diurnal variations in temperature are work, the partaking of meals, and exposure to various stimuli. In fever, the temperature may go up to 41° and 42° C., and in some cases even higher. The factors which influence the normal temperature curve, act in a much more pronounced way in the febrile patient, and the chart presents much greater diurnal fluctuations. The height of the temperature in fever in a great many cases is proportional to the intensity of the intoxication, and may serve as a measure for it. But in the two extremes of life, childhood and old age, it cannot be relied upon. Mild infections in the child

may be accompanied by very high temperature, whereas a most severe infection in the old, may produce a rise of only 1° or 2° C. (Krehl).[4]

The temperature of the normal individual is maintained at a constant level, because of the function of the heat regulating centre, which is situated in the anterior portion of the corpus striatum (Aronsohn und Sachs).[5] This centre stands in close nervous communication with every part of the body, and with all the vital centers in the medulla oblongata, especially the vasomotor centres.

All the vital processes in the cells of the body, be they secretion or motion, are the result of oxidation of organic matter in the cells. The oxidation of these substances is accompanied by generation of heat. This heat is utilized in keeping the body warm. It may be measured in terms of calories. One calory is the equivalent of the amount of heat that is necessary to raise one liter of water 1° C.

The human individual produces when at rest and under normal conditions, 33 calories per kilo. of his body weight every twenty-four hours. In other words, a man of 70 kilos will generate in the course of twenty-four hours, 2310 calories, that is, an amount of heat which will raise 23 liters of water from the freezing to the boiling point. Let this man do some work, and at once the oxidative processes will be increased, and more heat will be generated. All this heat is not retained in the body, but is given off into space. This is accomplished: (1) By radiation and conduction, and (2) by the evaporation of water from the skin and lungs.

It is at once apparent that the amount of heat lost by the body by radiation and conduction depends entirely upon the difference in temperature between the body and the surrounding atmosphere. To prevent the loss of too much heat in the lower animals, nature has supplied them with a coat of fur or feathers, which contain large quantities of stagnant air between. This stagnant air is a very poor conductor of heat. Civilized man resorts to an artificial method of protection against loss of too much heat. He covers his body with clothing, the character of which varies with the climate and the surrounding temperature. At this point we may accept without any reservation, the speculation of MacCallum[6] when he says, ". . . After all, it was this need of artificial heat regulation which probably brought about man's suddenly acquired knowledge of good and evil."

The temperature of the body can be maintained at a constant level only when there is complete calorific equilibrium, that is when the same quantity is eliminated as is produced. Should the heat elimination be greater than the heat production, there at once takes place a lowering of the body temperature. Should, however, the heat production be greater than the heat elimination, the tem-

[4] Das Fieber, Pathologische Physiologie, 1910.
[5] Pflüger's Archiv, p. 37.
[6] Arch. of Internal Medicine, 1909

perature will rise. The function of the heat regulating centre is to prevent these variations.

When a man is exposed to cold, a stimulation of the peripheral nerves takes place. This stimulation results in reflex contraction of the superficial bloodvessels. Less warm blood is brought to the skin, consequently, less heat is lost. Should the exposure continue and the physical process be inadequate for the protection against loss of heat, then a new factor is brought into play—the chemical process. All the muscles are thrown into fibrillary activity, shivering takes place, oxidation is thus increased, and a greater amount of heat is generated, enough to equal the loss. The body temperature remains unaffected.

If, however, the man is exposed to a tropical temperature, little or no heat can be lost by radiation and conduction, because the difference between the body temperature and the temperature of his environment is not great enough. A dilatation of the superficial bloodvessels and profuse perspiration takes place. This perspiration is evaporated, and every gram of water during the process of evaporation takes away 0.59 calories of heat from the body. We see from the experiments performed by Rubner[7] that a man, who was exposed to a temperature of 20° C., evaporated 56 gm. of water per hour. When he was exposed to a temperature of 36° to 37° C., his body temperature being equal to the temperature of the surroundng atmosphere, he could lose no heat by radiation and conduction. The amount of water then evaporated per hour rose to 204 gms. These 204 gms. of water per hour required 120.3 calories, to evaporate. For the twenty-four hours, a total of 2888 calories, the equivalent of the total amount of heat produced by that man. The man's temperature remained constant. This is a good illustration of how perfectly the heat regulating centre acts. It may be stated here, that R. Cohn succeeded in producing dilatation of the bloodvessels and secretion of sweat, by simply raising the temperature of the blood of the carotid arteries on its way to the brain.

The Mechanism of Fever. Having considered the physiology of the temperature regulation, we will take up the subject of the mechanism of fever. It is evident from what was said above, that the rise in temperature in fever can be accomplished only by a disturbance in the balance between heat production and heat loss. There are two possibilities, therefore. Either there is an increase in heat production without a corresponding increase in heat loss, or there is no increase in heat production, but there is diminution in heat loss. In either case a storing of heat in the body will take place. An enormous amount of work has been done on this subject in the past number of years, and the results are very conflicting, undoubtedly due to the differences in the methods employed by the

[1] Die Gesetze des Energieverbrauchs bei die Ernärung, 1902.

different investigators. Time does not allow us to enter in any detailed discussion of these methods and their respective results. I shall only summarize the work which is most complete and very convincing. This work was performed by Likhachev and Avroroff,[8] in Paschutins Laboratory, in St. Petersburg.

They studied the metabolism of a young Russian woman who was afflicted with malaria. She was placed in an oval shaped calorimeter which had a capacity of 2.7 cubic meters. She was made comfortable by being placed on a bed close to the floor. The calorimeter was kept hermetically sealed. Eighty liters of air were driven through the calorimeter per minute, and were made to pass through sulphuric acid for the determination of water, and through potassium hydrate for the determination of carbon dioxide given off by the patient. Before the experiment was begun, the patient was weighed, her food and water for drinking were measured out. After she had been installed and sealed in the calorimeter, ventilation was carried on for one to two hours until an equilibrium in temperature was established. The other twenty-two hours of the twenty-four were divided into eleven two-hour periods. At the end of every hour the patient's temperature was ascertained, also the temperature of the room, air, and of the calorimeter. At the end of every period the weight of the CO_2 and water given off were determined, also the amount of air that passed through the calorimeter and its temperature.

The heat lost by radiation and conduction was determined by noting the changes in the temperature of the calorimeter and the changes in the temperature of the air that passed through it. The heat lost by evaporation of water was measured by determining the quantity of water given off by the patient through her skin and lungs, and by multiplying same by 0.59 calories. The total heat production was obtained from the sum of the values of the heat lost by evaporation of water and by radiation and conduction plus or minus the retention or loss of heat because of changes in the body temperature. This last one was determined from the following formula: $W \times (T \pm t) \times S$. W equals body weight, T equals temperature of body, t equals value of change in temperature, and S equals specific heat of body, which equals 0.83.

The patient was kept in the calorimeter for three days, one normal and two febrile. The results are here tabulated. See table I and Figs. 1 and 2.

The patient was at perfect ease while in the calorimeter. We see from the curve of the normal day, that the heat production fluctuates from 85 calories per hour to 46 calories, and that the total heat elimination throughout the day runs approximately parallel to the former. We also notice that the greatest amount of heat,

[8] Isviesti Imperatorskoy Voenno Medicinskoi Academii, 1902, v, 239. I am indebted to Prof. F. G. Benedict for kindly calling my attention to this work, which was published in 1902, and remained entirely unknown to the western world.

74.6 per cent., is lost through radiation and conduction, and that only 25.4 per cent. is lost by evaporation of water.

On the day of high fever, at midnight the patient was placed in the calorimeter. During the morning, she presented the typical symptoms of malaria. At 1 A.M., the chill set in which lasted for about two hours. The heat production per hour thus rose from 54 calories to 93. The heat elimination, however, sank from 65 calories per hour to 57. This tremendous disturbance in the balance between

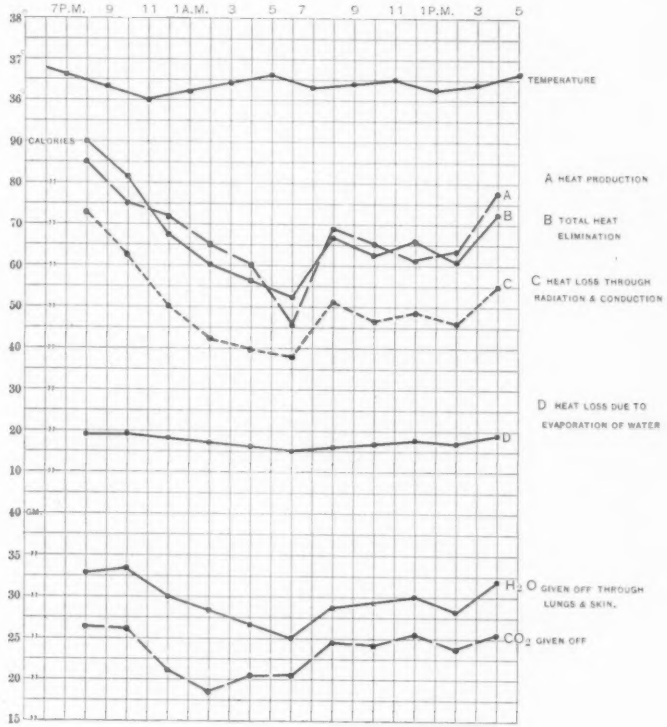

FIG. 1.—Normal day.

heat production and heat loss resulted in heat being stored in the body, and the body temperature rose from 36, to 38, 39, and finally to 39.7° C. These results led the experimentors to conclude that the rise of temperature in fever is due to an increase in the heat production without a corresponding increase in heat elimination.

This increase in heat production is most marked during the period of the initial chill. In long continued fevers, some authors believe there is an increase in heat production only in so far as there is an

increase in the activity of the respiratory muscles and heart beat. Matthes,[9] however, believes that after subtracting the heat produced by the increased activity of the respiratory muscles and increased heart beats, and by subtracting the increased heat produced, due to rise in body temperature, there will still be found an

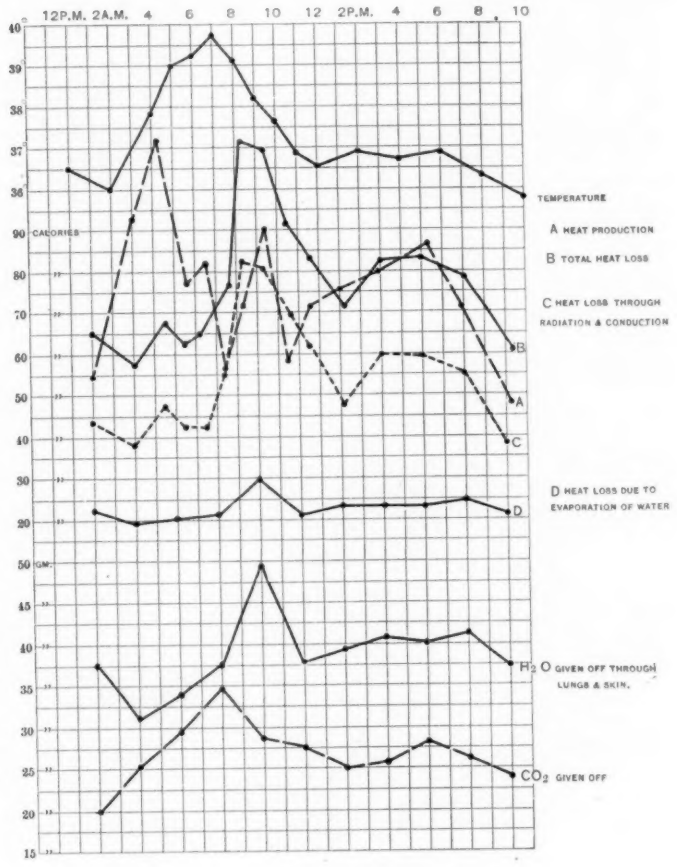

FIG. 2.—Day of high fever.

increase above the normal. This increase, he believes, is caused by the toxins themselves. As a matter of fact, Krehl and Soetbeer found an increase in heat production in infected cold-blooded animals.

[9] Ueber das Fieber; Die Deutsch. klin. am Eingange des Zwanzigsten Jahrhunderts, 1909, p. 1.

TABLE I.

Condition.	Total heat production. Calories.	Maximum heat production per hour. Calories.	Minimum heat production per hour. Calories.	Heat lost by radiation and conduction. Per cent.	Heat lost by evaporation of H_2O. Per cent.	Food value in calories.	CO_2 given off in grams.	H_2O evaporated from skin and lungs in grams.	O_2 consumed in grams.	R. Q.	Amount of urine. Grams.	N in urine.	C in urine.	Body temperature. (C.)
Normal	1480	91.0	53.0	74.6	25.4	1030	513.0	637.0	406.0	0.92	1796.0	11.4	8.8	36.0 to 36.7
Low fever	1492	78.6	56.6	74.7	25.3	776	520.0	638.0	474.0	0.8	442.0	9.1	7.5	
High fever	1633	112.0	48.0	69.8	30.2	533[1]	587.0	852.0	563.0	0.76	593.0	10.2	6.9	35.8 to 39.7

[1] The food taken on this day is almost one-half of normal. This influences heat production a great deal by eliminating the specific dynamic action of that food.

TABLE II.—Bacilli in 100 Leukocytes.

Temperature.	Typhoid B.	Streptococci.	Staphylococci.	Tubercle B.
36° C.	1080	1400	1210	1110
37 to 37.5	1100	1520	1200	1400
38.5	1120	1560	1590	1580
35.9 to 40	1530	1650	3100	1800
41.5	1040	....	1150	
42.5	610	760		

The cause of the accelerated pulse and respiration during fever can be found partly in the overheating of the body. But we must not exclude the possibility of a specific toxin acting on the cardiac and respiratory centres. The fact that the character of the pulse and its rate are different in different diseases, that it is always slow in typhoid, and very rapid in sepsis, speaks very much in favor of this possibility.

THE EFFECT OF HIGH TEMPERATURE. It was the belief of the early investigators (Liebermeister, Littern), that the high temperature in fever produced deleterious influences on the organism, and that the fatty and parenchymatous degenerations were due to it. This belief was practically universal, and in the matter of treatment of febrile patients, it was always borne in mind. The works of Naunyn[10] and Unverricht,[11] based upon clinical and experimental observation destroyed these theories. Naunyn showed that animals can be kept for weeks at a febrile temperature without presenting any signs of degeneration. As soon as this was corroborated and the conviction of the harmfulness of the high temperature removed, investigators began to inquire into the purpose of the high temperature in fever. The application of the Darwinian doctrine of the "preservation of the useful" to this case, was energetically opposed by Krehl,[12] who showed that this theory cannot be used in explaining pathological processes.

Rolly and Meltzer,[13] and later Lüdke,[14] studied the influence of the febrile temperature on the different components of the reaction toward infection. Namely, its influence: (1) On the growth of bacteria in the animal body; (2) on the resistance of animals toward bacterial infection; (3) on the bactericytic power of the blood; (4) on phagocytosis; (5) on the bacterial toxins; (6) on the production of antitoxins.

The hyperthermia was brought about by placing the animals in well ventilated, double-walled metal cages, which were kept at a temperature of about 35° to 36° C. by means of a burning flame. This flame was regulated by means of a thermoregulator which was situated between the walls of the cages. The animal's temperature under those conditions rose to about 40° C. The animals that were overheated, after receiving daily subcutaneous injections of one-fourth to one-half the fatal dose of either staphylococci, pneumococci, or bacilli coli communis, lived longer and one-half of them survived, whereas all of the control animals died.

The influence of the febrile temperature on phagocytosis is shown beautifully in Table II.

[10] Arch. f. Experimentelle Pathologie und Pharmacologie, 1884, xviii, 49.
[11] Deutsch. med. Wochenschr., 1883, vol. v.
[12] Lubarsch Ostertags Ergebnisse, 1896.
[13] Deutsch. Arch. f. klin. Med., 1908, xciv, 335.
[14] Ibid., 1909, xcv, 425.

THE TREATMENT OF FEBRILE CONDITIONS.[1]

By Frank Sherman Meara, M.D.,

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It is one of the most hopeful features of modern therapy that it is taking cognizance of the fact that the organism has been perfecting means of defense since first it became the seat of disease and that these means of defense are to be read not merely in the subtile elaboration of antitoxic bodies in the tissues and the marshalling of counter-forces in the blood elements, but also in the alteration of the functions of organs. Emesis as a symptom is primarily an effort to unburden the stomach of deleterious substances; diarrhea is protective in the same sense; cough removes secretions which are both irritants and mechanical impediments to the respiration; pain ensures rest to an affected part and so on. Interference with these symptoms must be undertaken with discretion lest it become pernicious. It is the knowledge of when to let alone and when to interfere that constitutes the art of therapy. Emesis, diarrhea and cough may become a source of exhaustion; pain which has pointed the way to the trouble and hinted the need of rest be illy borne when continued and fever arise to degrees that are incompatible with its purpose and constitute hyperpyrexia. At this point, treatment steps in to modify and assist, not to disregard Nature's signals.

Fever, as the physician knows it, is almost invariably the result of bacterial action, so cannot be dissociated from toxemia; but pyrexia and toxemia show but little parallelism; indeed, the worst forms of toxemia may be accompanied by no pyrexia at all, while a relatively high temperature may be seen with a minimal toxemia. Briefly, then, unless the degree of temperature is inordinately high, that is, constitutes a hyperpyrexia, the treatment of fever is not an antipyretic treatment but an antitoxemic treatment, and such fall of temperature as accompanies our efforts is incidental to them and not the object at which we aimed.

The treatment of fever involves the appreciation of certain broad principles that in the main are physiological. They are not numerous, but they are of fundamental importance. We shall take them up seriatim. (1) rest; (2) diet, including the ingestion of water; (3) fresh air; (4) water locally applied, that is hydrotherapy; (5) drugs; (6) hyperpyrexia. I think it little matters what name we give the febrile process or the organism inducing it. The procedures are much the same.

[1] Read before the Eastern Medical Society, New York City.

REST. It is a valuable form of mental exercise for a physician to pause occasionally and review some of the fundamental facts of physiology that are relevant to the problem in hand. First one should recall the fact that the sum total of the body's activities are but the expression of the conversion of potential energy of the food stuffs into these different forms of energies; that the body observes an accurate balance between the intake and output; that the law of conservation of energy obtains in the human body as well as elsewhere, and, therefore, when the intake is lessened, the expenditure should be diminished and useless forms of work should be avoided that useful purposes may be subserved.

All this means that in fever rest is imperative and that, as the body cells are expending energy in the elaboration of protective substances and the processes of repair are active in inflamed tissues, muscular unrest and muscular work should be avoided. Physiologists tell us that CO_2, an end product of the combustion of food stuffs in the production of energy may be taken as a measure of the energy of work and heat arising in the body and that the same man who during sleep eliminates 22 grams of CO_2 an hour will, when awake and exercising the greatest amount of muscular relaxation possible, eliminate 31 grams, and under conditions that we ordinarily term rest, such as most patients observe eliminates 38 grams. These figures are cited to call attention to what a relative term "rest" is.

Again, in fever, the vascular and other vital centres are all too often sought out and when we recall the lessened number of heart beats in recumbency and slight fall of pressure under the same circumstances we appreciate the economy exerted in behalf of these organs by rest.

Rest means something more than going to bed, though that is imperative. It means that the bed must be comfortable, so that energy shall not be wasted in the effort to maintain strained positions or avoid uncomfortable ones; it means competent nursing; it means measures directed at sleeplessness and at delirium. Mental rest is equally important, for though the loss of energy in the mental processes *per se* is minute, strained and restless muscles are the results of anxiety and concern, as, indeed, are perverted functions in many organs. Leave the sick room to the sick; exclude solicitous friends. Job's comforters, mourners before the fact. Avoid the introduction of business matters or domestic concerns, and let quiet and order reign. The contrast between a well-ordered, neat, cool, sick-room, and a hot stuffy room with six to ten visitors, gas-jets in full action and Babel and Chaos regnant is one of the most striking that can be witnessed.

DIET. Again let us appeal to physiology for facts. They are (1) That the amount of work done and the amount of heat given off by the human body each day is derived from the food taken in that

day or stored in the body from previous meals and that that store is not inexhaustible. (2) That the amount of energy supplied a man at rest each day amounts on the average to 33 calories[2] per kilo of body weight which in a man of average weight amounts to 2300 calories. (3) That a sick man at rest requires as many calories of energy as a well man. (4) That fever makes certain demands in excess of those obtaining in health, because the increased temperature *per se*, that is, pyrexia above 102° F. increases the output some 25 per cent. on an average, thus raising our caloric requirements to 40 per kilo or 3000 for the man of average weight. (5) That the toxins of disease are destructive of body tissue in varying degrees, a destruction which may be overcome or minimized by a sufficient intake of food. (6) That the amount of proteid needed each day in health is about 100 grams. (7) That in fever the requirement is about the same or may be a trifle less, 75 to 85 grams, which is enough to prevent proteid loss when enough carbohydrates are added. The appreciation of these facts is increasingly important in the prolonged fevers, such as typhoid, certain bronchopneumonias or septic conditions.

One other fact is of special importance in orientating us correctly with reference to this subject; namely, that such studies as have been undertaken to determine the efficiency of the processes of digestion and assimilation of the foodstuffs in fever show that except at the onset these processes are scarcely impaired.

A sufficiency of food is an important item in the treatment of fever, because, as has been intimated already, an insufficiency leads to destruction of the body substance with the production of toxic material in the process, an autointoxication.

Briefly, in the beginning of fever, do not push the food; respect the meaning of anorexia; but later increase daily to the approximation of theoretical needs. Remember that there are other foods than milk that are easily digested, including cereals, bread, butter, eggs.

Water is an important item in the treatment of fever; all the water that the patient wants and his wants should be determined by offering him water at frequent intervals, as his cerebral condition may be such as to prevent his asking for the amount he needs.

Studies of the water intake in certain infections such as pneumonia show that the amounts are sometimes extraordinary, 3000 to 5000 c.c. a day, and that the patients who are given a sufficiency seem to do best.

Fresh Air. That the sick require fresh air would seem a thesis too simple to require emphasis, and yet many physicians make no protest against the vitiation of the sick room by a swarm of visitors and burning gas-jets and make only a half-hearted appeal for an open window.

[2] A calory is that amount of heat that will raise one kilo of water through 1° C.

The bad effects of ill ventilation are due largely to the accumulation of CO_2 gas. In the country pure air contains about 3 volumes of the gas to 10,000 volumes of air. In rooms and work-shops it may rise to over 30 volumes, and in the night with the gas burning to nearly 50.

We consider it niggardly in the hospital if we do not allow 1000 cubic feet to each sick infant, but how many of our patients get 1000 cubic feet of fresh air to themselves in the sick room.

The increase of CO_2 is not the only evil in ill ventilation, for contamination of the air with bacteria and varied forms of dirt must ensue; while, heat, moisture, and odors add their depressing effects.

But there is another quality to fresh air when taken in the open that adds materially to its value; it is the element of cold given either by the temperature of the air or by the effects of its movement. Pembrey, in a masterly article on Respiratory Exchange in Hill's *Recent Advances in Physiology and Biochemistry*, says "The success of the open-air treatment depends it would seem, not so much upon any greater purity of the air as upon free exposure; the open air increases the combustion and respiratory exchange improves the appetite and augments the metabolism."

More than that, it is an every-day demonstration to the students in our ward that the exposure of the febrile patient to the open air will induce a rise of blood pressure over that obtained in a well-ventilated ward equal to or better than that obtained from our usual vasomotor stimulants, with the added advantage of being continuously sustained which does not obtain with the drugs.

I am convinced of the very great value of the open air treatment of fever. The pulse and respiration improves, the cerebral intoxication diminishes and the patients are almost universal in their commendation of it.

To reap success, however, the technique must be correct. The patient's bed must be so made as to keep the body always warm, by enclosing the bed in impermeable material like rubber sheeting or paper, the use of the hot water bottle, and by sheltering from winds. The good effects, I believe, come from the action of cold on the nerves of the mucous membrane of the nose or of the face, producing reflexly an improved vascular condition.

Water Locally Applied, Hydrotherapy. I am firmly convinced of the efficacy of remedial measures, operating on the various functions through the surface of the body, that branch of the healing art included under the head of physical therapy. This field has been grossly neglected for various reasons; in part because of the dominant position occupied by drug administration in the minds of most practitioners and very largely because of the time and effort entailed in the administration of these measures and the acquisition of a proper technique.

Water is a very valuable instrument in combating the evil results of fever. Baruch, whose persistent advocacy of hydrotherapy constitutes a real service to American Medicine and has not received half the recognition it deserves, points out that the value of water lies not so much in its physical constitution as in the fact that it is an admirable material for the conveyance of heat and cold and that strickly speaking, thermotherapy is a better term than hydrotherapy in the use of water. A few facts should be borne in mind in considering hydrotherapy. (1) That we are aiming rather at the toxemia than at the pyrexia. (2) That the reaction to the use of cold water is the *sine qua non* of success. (3) That friction is as important as the cold in many of the procedures.

The good effects of the cold water are obtained largely through the nervous system. The impulses pouring in through the countless nerves upon the centres result in a slower, stronger heart beat, and an improved vasomotor tone, which can be measured in terms of an increased blood pressure; respiration is deepened, cerebral processes improved, and metabolism enhanced.

Without detailing the various procedures, one may mention as the best known, the Brand bath in typhoid fever and the chest-compress in pneumonia.

Through the cold air and cold water we effect much the same results; the time of year, the facilities of the environment and the reaction of the patients determine an indication for one or the other.

Drugs. Drug administration, like the other measures, is aimed not at the pyrexia but at the toxemia, and that the fever is influenced is due to a relief of the toxemia or the conditions determined by it.

Cathartics occupy an important position among the drugs, because they prevent a stagnation within the bowel and the consequent absorption of putrefactive products.

The toxins of disease impinge upon the vital nervous centres and upon none more certainly than upon the vasomotor centre. Our great dread in the severe intoxication, such as typhoid fever, pneumonia, diphtheria, scarlet fever, and sepsis is a circulatory failure. The term "circulatory" is used advisedly, because upon this we can all agree, but when we try to fix this failure in the heart or in the vasomotor apparatus an abundant opportunity for difference of opinion arises.

My own belief is that the careful studies of this question show that in the large majority of cases it is the vasomotor mechanism that is at fault. For this reason my preference is for drugs that act either on the vasomotor centre or on the vessels. My own choice at the present time is for caffeine and I think it should be given in sufficient dosage and so administered as to guarantee its arrival at the goal desired. I give it in the form of one of the soluble double

salts, that of caffeine and sodium benzoate or caffeine and sodium salicylate, in doses of five grains every four hours, and such studies as I have made upon its effects on blood pressure show that its effects do not last even throughout this period. Next to caffeine, I use a 10 per cent. or 20 per cent. solution of camphor in olive oil and use more than the usual dose, giving at least five grains every four hours, hypodermically, often alternating with the caffeine, thus giving a dose every two hours. Personally I have less faith in strychnine.

That we can exclude the heart in all cases I do not believe and so, if the vasomotor stimulants are not efficacious, one uses digitalis in doses of one-half an ounce of the infusion three or four times a day and appreciating that it will not become operative in less than twenty-four hours, may use as an initial dose one-half milligram of strophanthin intramuscularly.

No mention has been made so far of the antipyretics. In the early stage with bounding pulse, aconite may afford some relief by slowing the heart through the vagus, the coal tars may be used with relief of headache and other pains, but here again the fall of temperature is incidental. These drugs are depressants and should never be used where the circulation is impaired.

Hyperpyrexia. As has been said, fever may be looked upon as of purposeful intent, as a conservative effort on the part of the organism to accomplish something useful to itself. If this be so, measures directed at the fever as such are misdirected if not pernicious, and it will be noted that the treatment of fever outlined in this paper has been directed at the toxemia accompanying the febrile movement rather than at the latter; but as was said in the beginning, any symptoms primarily useful may in the end become harmful; one may say that Nature has overshot the mark. Excessive temperatures fall into this category as well as prolonged sustained temperatures.

Hyperpyrexia threatens cell function and cell integrity as increased proteid destruction shows. We see its effects best in insolation and in certain rheumatic fevers. In these cases reduction of heat is life saving.

We have no better method than the direct application of cold in the shape of cold baths or ice rubbed upon the surface of the body. The patient may be put into a bath of 90° F. and the water cooled down to 70° F. to 75° F. The body is kept immersed until the body temperature falls below the danger point, but it is wise to remove the patient when it falls to 102° F., as collapse may ensue on efforts to reduce it to normal. If such occurs, stimulants and heat are indicated, as in collapse from any other cause.

Antipyretics of the coal-tar group are not comparable in efficienyc or safety to cold water, but may be used where it is impossible to use the latter.

No attempt has been made in this paper to go into details; only generalizations have been laid down with special emphasis given to those branches of therapy commonly neglected, and for this reason serum therapy, which is specific for individual disease has been omitted.

CYSTS OF THE SPLEEN.

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The following case occurred in the Pennsylvania Hospital, upon the service of Dr. John H. Gibbon, during my term of service there, and on account of the rareness of the condition, is though of sufficient interest to report.

The patient, B. G., a female, aged twenty-five years, first noticed seven years ago, a slight swelling in the left side of abdomen and under the ribs in the splenic area. Since then this mass has gradually enlarged down, into, and across the abdomen. During the last year the growth was much more rapid, so that the tumor reached across the abdomen to a line drawn upward from the right iliac spine. Patient did not remember ever having been hit or struck in the region of the spleen. She complained of soreness over the mass, with at times slight nausea, but no vomiting, which was attributed to the mass. Her general health remained about the same as previous to the discovery of the tumor, but in the last year on account of the more rapid increase in growth, she though she had grown weaker. Her appetite was good, bowels constipated. She menstruated first at thirteen. Since then it has always occurred regularly with some pain the first day.

Her past medical history, family, and social history had no bearing upon the present condition.

The physical examination showed the patient to be a rather thin, somewhat anemic looking young Irish woman. Her complexion was pasty. Her teeth were in splendid condition. The lungs were normal. The cardiac dulness extended from the first interspace above, to the right border of the sternum on the right, and on the left, to the fourth rib directly below the nipple. The sounds were regular and with a good muscle tone, except that at the apex a soft mitral systolic murmur was heard. The abdomen showed the presence of a large tumor. This was largest and most prominent in the epigastrium. It was hard and in the upper part there was a distinct wave of fluctuation. This tumor extended above from the beginning of cardiac dulness, down the midaxillary line to within two inches of the anterior superior spine, then out one and one-

half inches to right of the umbilicus and then up to just within the liver dulness. The mass was movable on respiration and seemed to be the spleen or a cyst of the spleen. The left border was sharp and distinct, the right was dull and hard to determine. The liver dulness extended from the fifth to the eighth rib. The organ was not palpable. There was no change in the lymphatic system except that a few glands, small and discrete, could be felt in the cervical and the inguinal regions. Knee-jerks were not elicited.

The blood count was as follows: Red blood cells, 4,360,000; hemoglobin, 70 per cent.; leukocytes, 9400. The differential count showed polymorphonuclears, 65 per cent.; lymphocytes, 29 per cent.; mononuclears, 2 per cent.; transitionals, 1 per cent.; eosinophiles, 3 per cent.

On admission, the urine had a specific gravity of 1030. It contained a slight trace of albumin, but no casts, pus, nor sugar. Immediately before operation, the urine contained no albumin and was normal in every respect.

The operation was performed on September 14. Morphine, atropin, ethyl chloride, and ether were the anesthetics employed. An incision was made over the left upper rectus, the fibers of which were split. Upon opening the abdomen, a large cyst was found adherent to the diaphragm and surrounded, except in the upper part, by splenic tissue. This was freed from all surrounding adhesions and then tapped. Clear yellow fluid was removed, 100 ounces in amount. The splenic vessels were then tied off and the whole huge cyst and spleen amputated. With a great deal of difficulty about a half dozen bleeding places in the adhesions were tied off and all hemorrhage completely stopped. The peritoneum was closed with continuous catgut. The fasciæ were similarly closed, and a subcutaneous stitch put in, the edges of the wound being accurately approximated with sterile strips of zinc oxide adhesive.

The patient reacted fairly well. She had very slight postoperative nausea and no vomiting. Immediately after operation, her urine had a specific gravity of 1035. There was also a faint trace of albumin, but no casts nor blood.

The day after operation, the patient had considerable pain, particularly along the course of the diaphragm. This seemed much relieved by a broad adhesive strip along the diaphragm borders. Two days later her condition was good, though she had considerable abdominal distention. Two days later her condition continued good. She still had a little elevation of temperature, accounted for by several small abscesses under the adhesive strips. Eight days later she was improving rapidly, the skin wound was clean and completely healed. The patient had absolutely no subjective complaints, though she still had slight fever at times. Her blood count was as follows: Red blood corpuscles, 4,642,000; hemoglobin, 90 per cent.; leukocytes, 11,400; polymorphonuclears, 70.6 per

cent.; lymphocytes, 14.6 per cent.; mononuclears, 10.2 per cent.; eosinophiles, 2.4 per cent.; transitionals, 2 per cent.; basophiles, 0.2 per cent.

Two weeks after the operation patient was up and walking around. Her condition was very good. Her third blood count, eighteen days after operation, showed: Red blood corpuscles, 3,916,000, hemoglobin, 78 per cent.; leukocytes, 13,900; polymorphonuclears, 60 per cent.; lymphocytes, 24 per cent.; mononuclears, 11 per cent.; transitionals, 5 per cent. A little less than a month after operation she was discharged cured.

The condition of the patient at the present time, nine months after operation, is excellent. She has gained in weight, and in every way her general condition is good. Physical examination shows a scar well healed; no pain or tenderness anywhere in the abdomen; nor can any abnormalities be palpated. No enlargement of the superficial lymph glands is found beyond a few small discrete glands noted before operation. This, however, is to be expected, as such an enlargement would probably take place only in the hemolymph glands.

The recent blood count is as follows: Red blood corpuscles, 4,400,000; hemoglobin, 80 per cent.; leukocytes, 17,700; The differential count of 200 cells shows: Polymorphonuclears, 70 per cent.; lymphocytes, 25 per cent.; mononuclears, 3 per cent.; transitionals, 1 per cent.; eosinophiles, 0.5 per cent.; undetermined, 0.5 per cent.

Pathological Descriptions. The specimen consists of a spleen at the upper margin of which a huge cyst has been opened and collapsed. The entire specimen weighs 400 grams. It is more or less rounded and measures about 18 cm. across. The cyst occupies the upper posterior region of the spleen, so that the spleen forms a semicircular wide rim, 6 to 8 cm. across the lower and anterior margin of the cyst, and is surrounded on three sides by spleen tissue. Excluding the cysts, the spleen itself is much enlarged. The surface of the cyst is fairly smooth, but is covered here and there with fibrous tags (see figure). The spleen is dull purplish red in color, and is of medium consistency. The cyst contained at operation a large amount of yellowish-brown fairly thin fluid, containing a considerable amount of cholesterin crystals. The covering of the cyst is white and opaque. When opened it is found to be a single cavity, almost the size of a football. On the inner surface, however, it is quite smooth, reddish in color and shows in many places yellowish masses which look like cholesterin crystals. The wall measures about 5 mm. in thickness. The spleen on section shows a smooth reddish-gray surface. The Malpighian bodies are visible. The trabeculæ are not prominent. The cyst wall comes in such close approximation to the spleen that it appears to be an integral part of the organ.

Microscopic Examination. Sections through the spleen pulp. The pulp contains very little blood. The venous sinuses are all well defined, and there seems in places to be some increase in the connective tissue of their wall. The tissue appears very cellular, and many of the venous sinuses contain a few polymorphonuclear leukocytes and small round cells. The malpighian bodies are large. The germinal centres are swollen. About the periphery one occasionally sees uninuclear giant cells of epithelioid type. The trabeculæ are not especially prominent. The wall of the cyst is formed of dense connective tissue containing few cells and appearing in places almost hyaline. There is little cellular infiltration but here

Spleen containing cyst that has been opened.

and there a few small bloodvessels are seen between the connective tissue fibers. Occasionally a few isolated plasma cells, epithelioid cells, or small round cells are seen between the strands of dense connective tissue. In one section free blood is also seen between the fibers. The wall of the cyst is not lined by cells.

Anatomical Diagnosis. A cyst with dense connective tissue wall, either arising about the capsule of the spleen or in the spleen itself.

Examination of the Cystic Fluid. Specimen consists of 75 c.c. clear straw-colored fluid, in which are fine, transparent, yellowish particles. Reaction, alkaline; specific gravity, 1030; albumin, 13 per cent. Microscopically many cholesterin crystals are found. Inoculation of various culture media proved negative.

Cysts of the spleen may be classified as follows: (1) Dermoid; (2) echinococcus or parasitic; (3) non-parasitic, (*a*) unilocular, serous, hemorrhagic, lymphatic; (*b*) multilocular.

Of the first variety of cysts, but one has ever been described, the classic case of Andreal,[1] reported in 1829.

The second variety is rare but commoner than the other varieties, and is most frequently found in those countries subject to hydatid disease. In proportion to the number of hydatid cysts occurring in other parts of the body, the incidence of hydatid of the spleen, according to different authorities,[2] is from 2 per cent. to 3½ per cent. of all cases. These, for the most part, have been treated by incision and drainage, but numerous cases have been treated by splenectomy. Johnson,[3] in 1908, collected 23 cases thus treated, with 4 deaths. Since then none has been reported, although Gill[4] reports a case with postmortem, occurring in England, of a Portuguese laborer, who died as a result of a huge hydatid cyst of the spleen.

The third variety, non-parasitic cysts, both clinically and when accidentally found at the autopsy table are very rare. Powers,[5] in 1906, found 32 cases of non-parasitic cyst reported in the literature. Johnson,[6] writing two years later, added 6 more cases, while Bircher[7] finds 33 cases of cyst treated surgically. Since then 4 other cases have been described. The case Bircher reports, he treated by resection with fatal termination. He also quotes the case of Hedinger in which splenectomy was done. Huntingdon[8] reports the third case, and Fowler,[9] the fourth, although the latter's case was not a typical serous cyst, but consisted of a spleen riddled with small cysts, in which the diagnosis of lymphangioma was made.

At autopsy, Henrieius[10] says, the condition is rarely found, and mentions 6 cases in the literature of serous and non-parasitic cysts. Concerning the pathogenesis of serous cysts of the spleen, several theories have been advanced.

1. Many serous cysts have unquestionably arisen from hematoma. This may be due either to a rupture of a normal splenic vessel, most frequently subcapsular from trauma, or to the rupture spontaneous or traumatic, of a diseased bloodvessel, with extravasation of blood into the splenic pulp and later encapsulation. The solid constituents of the blood are, says Moynihan,[11] deposited in

[1] Grundriss der path. Anat., 1830, p. 257.

[2] Thomas, Allbutt's System of Medicine, iv, 456; Litten, Diseases of the Spleen, Nothnagel's Encyclopedia.

[3] Annals of Surgery, 1908, xlviii, 50.

[4] British Med. Journal, 1910, i, 1545.

[5] Annals of Surgery, 1906, xliii, 48.

[6] Loc. cit.

[7] Deut. Ztsch. f. Chir., 1908, xcii, 323.

[8] Trans. Amer. Surg. Assoc., 1907, xxv, 336.

[9] Surg., Gynecol., and Obstet., 1910 xi, 133.

[10] Arch. f. klin. Chir., 1904, lxii, 138.

[11] Quoted by Johnson, loc. cit.

lamina upon the walls of the cyst, the fluid contents thereby becoming clearer.

2. Non-parasitic cysts of the spleen may arise from changes in lymphangioma, as in the case of Fowler.

3. The theory has been advanced by Ranggli,[12] that cysts of the spleen arise from infoliation of the peritoneal endothelium, subsequently stimulated to growth and cyst formation.

4. Beneke[13] believes cysts of the spleen may arise from rupture of the capsule with protrusion of the splenic pulp, the latter proliferating and subsequently becoming cystic.

5. Litten,[14] quoting Böttcher, thinks there is a softening of the pulp with necrosis following occlusion of vessels due to amyloid degeneration.

Mueller,[15] in a recent paper, has gone extensively into the subject of pathogenesis of small cysts of the spleen, and has found them in 11 per cent. of his series of autopsies. Of the large unilocular cysts, he says, without further study and from the lack of experimental work, no definite causative factor can be given.

The present case, although giving no history of trauma, is probably hemorrhagic in origin. The walls of the cyst are more or less laminated, and old blood pigment is found in the cyst wall. The contents were albuminous and of a high specific gravity.

Pathology. The contents of the unilocular cysts may be either serous, hemorrhagic, or chylous. In the first type the fluid is clear, yellowish in color with a low specific gravity, as a rule from 1005 to 1010; albumin may or may not be present, while cholesterin crystals are invariably found. In the second type blood is found, the fluid is turbid, the color varies from a yellow red to a dark brown red, while albumin is always present. Microscopically red blood cells and cholesterin crystals are always seen. In the third type, lymphatic cysts, the specific gravity is much higher, the fluid is turbid and grayish white in color. Microscopically red blood cells, lymphocytes, and cholesterin crystals are found.

Unilocular cysts may vary much in size and have been reported up to the size of a football. All those found at operation have been large. They are surrounded by chronic inflammatory tissue and attached more or less firmly to the surrounding tissues by adhesions. The wall of the cyst is dark in color and varies from 2 to 5 mm. in thickness. The splenic parenchyma may be entirely destroyed or only that of the pole from which the cyst arises, usually the lower pole. The inside of the cyst wall is, as a rule, laminated and divided by thick ridges, and in its fresh state is smooth and glistening. Microscopically the walls are found to consist of dense con-

[12] Inaug. Diss. Zurich., 1894.
[13] XIII Internat. Kongres für Medizin, Paris, 1900, p. 317.
[14] Loc. cit.
[15] Arbeiten a. d. Geb. d. path. Anat. u. Bakter., Tübingen, 1910.

nective tissue, lined with endothelium, and containing blood pigment.

It is the opinion of Monnier,[16] that the majority of non-parasitic cysts occur in women, usually during the menstrual cycle. The large number in menstruating patients is due to hyperemia and consequent relaxation of the period. In the reported cases, the age of the patients varies, but no cysts have been reported in individuals under seven years of age, and only three under fifteen years.

The fact that so few patients were under fifteen years of age would seem to make developmental fault a rare factor in the causation of the condition, while on the other hand, the history of trauma in so many cases shows conclusively that there has been at some time an injury to a splenic bloodvessel.

Symptomatology. In most cases the symptoms are those of a slowly growing tumor in the left hypochondrium. As the tumor increases in size, pressure symptoms, or symptoms due to the mechanical weight of the mass, may develop. These are evidenced by digestive disturbances, flatulence, at times nausea and vomiting as the result of pressure on the stomach, and constipation, from pressure on the bowel. This is well illustrated in my case, as practically the only subjective symptoms were nausea and constipation. A sense of soreness may also be noticed over the mass, while pain, from mechanical traction, referred toward the left axilla and shoulder, is also frequently present. Added to this is always a sense of discomfort. This was also noticed in the present case, and was to be expected, considering the size of the mass, which extended down and well over to the right of the umbilicus and filled completely the epigastrium and left hypochondrium. Objective symptoms are those of any large mass. The site of occurrence, the fact that the tumor dulness is confluent with the splenic dulness, the direct connection frequently found with the spleen by palpation, and the moving of the mass with respiration, all point to the spleen as the site of the origin of the tumor. The cystic character of the tumor is readily recognized by the waves of fluctuation, easily elicited.

In the blood before operation no marked changes have been observed, but the postoperative changes in the blood from splenectomy have been many and varied. In those cases reported with full blood counts there has always been noted a decrease in the hemoglobin and red blood cells with leukocytosis. Some observers have found lymphocytosis, others an eosinophilia, others, the presence of many large mononuclears with a gradual return to the normal differential count in a period of from three to six months. In the present case, shortly after the operation, a considerable increase in the relative number of large lymphocytes occurred,

[16] Beiträge zur. klin. Chir., 1903–04, xli, 181.

but the examination recently made does not show this, although there is still a persistent leukocytosis.

Treatment. In regard to operative procedures in cysts of the spleen a variety of means has been used in the past, as injection with iodine, drainage, and so on. Apparently only three methods are now employed: (1) Resection of cyst, (2) drainage or drainage with marsupialization, and (3) splenectomy.

Bircher finds 4 cases treated by resection of the cyst, with 1 death, due to postoperative ileus. Two others are reported by Powers, making a total of 6 treated by this method. Of the second method, 8 cases have been reported, with one death.

Splenectomy for serous cysts of the spleen has been performed, according to Johnson, nineteen times up to 1908. An additional case has been found by Bircher, the case of Hedinger. Fowler's case was also treated by splenectomy, although not a serous cyst. The case I have just described, operated upon by Dr. Gibbon, brings the list up to 21 with no fatalities.

In conclusion, I wish to express my thanks to Dr. Gibbon for permission to report the case and Dr. Longscope for the pathological description.

A CASE OF LATE HODGKIN'S DISEASE (LYMPHOMA GRANULOMATOSUM), WITH REMARKS ON VARIOUS CASES PRESENTING THE CLINICAL PICTURE OF SPLENIC ANEMIA (BANTI'S DISEASE).[1]

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The patient, H. A., aged twenty-seven years, a German hairdresser in London, was admitted to the German Hospital, on September 29, 1910. Though I saw him once, myself, in February, 1909, I am chiefly indebted for the previous history of the case to Dr. P. P. Daser, under whose care the patient had been before admission to the German Hospital. There was a doubtful history of syphilis about 1905, but the present illness apparently commenced in November, 1908, with a swelling of the right side of the neck, which increased fairly rapidly in size, though it caused no pain. On February 1, 1909, the patient appeared slightly anemic, but fairly well-nourished, weighing 120 pounds. On the right side of his neck was a movable tumor about the size of an apple, situated beneath the middle third of the sternomastoid muscle and apparently formed by a mass of discrete, enlarged, lymphatic glands.

[1] Read before the Medical Society of London, April 10, 1911.

Smaller nodules could be felt lower down in the neck on the same side and some also on the left side. No enlargement of the lymphatic glands elsewhere was detected. A blood film (February 16, 1909) showed slight leukocytosis.

The patient was treated by intramuscular injections of an arsenical preparation, soamin, about every third or fourth day, and at first he seemed to improve. On March 12, 1909, the glandular protrusion on the right side of his neck was scarcely noticeable by sight, though the glands could still be felt. Then he suffered from fever, vomiting, and general malaise (no diarrhea), and kept to his bed for a time. A doctor who attended him thought he had influenza. On April 3, 1909, he looked paler and thinner, weighing only 108 pounds, and the lymphatic glands again had increased in size. Moderate enlargement of the axillary and inguinal lymphatic glands could likewise be detected. There was no ascites and neither the spleen nor the liver could be felt. Iron and a simple tonic medicine were prescribed. He gained in weight and apparently felt better, but after April he did not come under observation again for a considerable time. He was apparently not taking arsenic. In December, 1909, he wrote that he had a febrile attack, similar to that of March, 1909. This weakened him, but was accompanied or followed by the almost complete disappearance of the swelling on the right side of his neck. Two weeks afterward, however, the lymphatic glands began again to increase in size. When seen on September 26, 1910, he said that for the last five weeks he had been ailing, with loss of appetite, fever, and emaciation. He looked thin and pale; his temperature was 104.6° F., and his pulse 120 to the minute. The lymphatic glands could be felt enlarged, but were smaller and harder than when he was first seen, in February, 1909. The liver and spleen were both enlarged, especially the latter, which was hard and slightly tender to palpation. The urine was free from albumin and sugar. Blood films showed distinct leukopenia.

He was admitted to the German Hospital on September 29, 1910, and there his pyrexia and cachexia continued. The fever was of an irregular septic type, the temperature generally varying between 100° and 103° F. The pulse was frequent and weak. Ascites and jaundice developed in the second half of October, and the jaundice gradually increased in intensity. The feces were pale and the urine contained bilirubin, as in cases of obstructive jaundice.

On November 15, 1910, I noted that he was very feeble, jaundiced, and emaciated, with smooth and uniform enlargement of the spleen and liver. The spleen reached downward to just below the umbilical level. The hepatic dulness commenced above at the sixth rib in the right nipple line, and the lower edge of the liver could be felt at about the umbilical level. The heart and lungs showed nothing special. The tongue and mouth were very dry.

The lymphatic glands in the neck could be felt slightly enlarged, but the axillary glands could not be felt at all, and those in the groins were hardly larger than they are in many normal individuals.

Death occurred in a condition of collapse on November 23, 1910. The fever had continued up to the middle of November, but during the last days of life the temperature was usually subnormal and there was a good deal of diarrhea. The urine, when tested about that time, contained 1 per mille albumin. There was little ascites, but a good deal of edema. A few purpuric marks were seen on the abdomen, in lines, as if he had scratched himself, but the jaundice was never accompanied by definite pruritus.

In the hospital, von Pirquet's cutaneous reaction for tuberculosis had given a negative result; so had Widal's reaction. Wassermann's seroreaction for syphilis, performed by Dr. H. R. Dean, at the Lister Institute, was likewise found negative.

A blood examination by Dr. G. Dorner, on September 30, 1910, gave: Hemoglobin, 56 per cent.; red cells, 3,333,330 in the cubic millimeter; color index, 0.86; white cells only, 2480 in the cubic millimeter; no eosinophilia. A differential count of 500 white cells (October 25, 1910) gave: Polymorphonuclear leukocytes, 84 per cent.; small lymphocytes, 3 per cent.; large lymphocytes, 1.7 per cent.; large mononuclears, 7 per cent.; transitionals, 4.3 per cent. Only one nucleated red cell was seen during the count of 500 white cells. The red cells showed anisocytosis and moderate poikilocytosis, as in secondary anemias. On November 12 the hemoglobin was only 35 per cent.; red cells, 1,910,000 in the cubic millimeter; color index, 0.9; white cells, 4124 in the cubic millimeter.

Necropsy and Microscopic Examination. Body much emaciated and jaundiced. The brain and cerebrospinal fluid are not bile stained. The brain weighs 42 ounces and shows slight apparent atrophy of the convolutions. The pericardium contains about 70 c.c. of clear bile-stained serous fluid. On the heart (weight, 9 ounces) are a few pericarditic patches; there is some old thickening of the mitral valve. No atherosclerosis of the aorta or coronary arteries noted. There is chronic indurative pneumonia (as proved by subsequent microscopic examination) of part of the middle and upper lobes of the right lung. Both lungs show hypostatic edema. Pleuritic adhesions are present on both sides. No pulmonary tuberculosis. The peritoneum contains 2400 c.c. of somewhat turbid, bile-stained, ascitic fluid, which is found by microscopic examination to owe its turbidity to the presence of fairly numerous white corpuscles. No evidence of tuberculous peritonitis.

Spleen. Weight, 32 ounces. Uniformly enlarged; rather hard; surface smooth, but showing patches of perisplenitic thickening of the capsule; also one or two scars, which on section are found to be connected with small anemic infarcts. The splenic substance is of a red color and contains numerous small miliary to pea-sized, pale nodules, and a few small hemorrhages.

Liver. Weight, 66 ounces. The surface is smooth and even, with the exception of a little old patchy perihepatitis; it is of greenish color with scattered spots of red. On section, the hepatic substance is found to contain a few pea-sized pale nodules. The red spots beneath the capsule are evidently due to the presence of similar minute nodules, into which hemorrhage has taken place. The common bile duct during life was probably obstructed by a large, chestnut-sized lymphatic gland in the hilum of the liver, but at the necropsy, by firm pressure on the gall-bladder, some bile can be squeezed out through the ducts into the duodenum.

In the kidneys, which weighed together 12 ounces, a little patchy greenish coloration observed in the cortex has been found by subsequent microscopic examination to be probably due to the presence of bile-stained casts in the renal tubules. Nothing special noted in the suprarenal glands, pancreas, stomach, intestines, thyroid gland (rather large), prostate, testes, urinary bladder, abdominal aorta, or great abdominal veins.

The lymphatic glands are widely affected in the thorax and abdomen. Some of the bronchial glands, which are pigmented, are of about the size of large cherries, and the glands in the posterior mediastinum, close to the spinal column, are likewise enlarged. The mesenteric glands vary from the size of a pea to that of a chestnut, some near the spleen and at the hilum of the liver being specially noticeable. One, as large as a chestnut, in the hilum of the liver is hard, colorless, and almost translucent on section. Several of the lymphatic glands in the neck are as large as a hazel-nut. No matting together of lymphatic glands, as in tuberculosis, observed anywhere.

The bone marrow examined in the shaft of the left humerus is red, with small white nodules in it.

I am greatly indebted to Dr. J. C. G. Ledingham for the following report of the microscopic appearances: A lymphatic gland. The fibrosis of the reticular structure of the gland characteristic of the later stages of Hodgkin's disease (lymphoma granulomatosum) is so far advanced that only small patches of lymphoid tissue remain. Some of these, however, present the typical epithelioid cells and giant cells found in Hodgkin lesions. The giant cells have, as a rule, vesicular nuclei, but in some cases the nuclear chromatin is markedly pyknotic. In the interstices of the fibrotic areas plasma cells are exceedingly numerous, but the great majority show lobing and karyorrhexis of their nuclei. Some giant forms of plasma cells are also present. No necrotic areas are seen on section. Other lymphatic glands examined are characterized mainly by fibrotic changes, typical lymphomata with giant cells being absent. Eosinophilic foci are not found. Many of the perivascular lymph spaces contain large numbers of streptococci. They do not appear in the lumina of the bloodvessels.

Spleen. The structure of the spleen is essentially similar to that of the lymph gland, except that the fibrosis is still further advanced and necrotic areas are present. Normal lymphoid nodes (Malpighian corpuscles) are very scarce, but here and there a typical lymphoma is found with epithelioid and giant cells. The necrotic areas are surrounded by numerous effused blood corpuscles and cells containing hemosiderin are very frequent. Small calcified areas staining well with hematoxylin occur in some of the vessel walls and in the necrotic portions. The sinuses contain large numbers of desquamated endothelial cells.

Liver. The liver nodules resemble the spleen in structure. They have evidently been derived from lymphoid structures in the portal areas. Fibrosis is well advanced, but occasional lymphomatous nodes are left, containing scanty giant cells. The bile ducts seen in the fibrotic areas show well-marked proliferation of their epithelium, Dr. Ledingham had observed this in one of his own cases.

Bone Marrow. This is essentially myeloid in structure, the great majority of the cells present being neutrophilic and eosinophilic myelocytes. Normoblastic foci are very numerous. The white nodule examined in one of the sections is found to be a necrotic area from which practically all the cellular elements have disappeared.

Sections of liver, spleen, and lymphatic gland, specially stained with methyl-violet, show the presence of a certain amount of amyloid change.

Remarks on the Nature and Diagnosis of Hodgkin's Disease. The present case is, therefore, as the examination after death proves, undoubtedly one of Hodgkin's disease, or, to give this disease some of its synonyms, lymphadenoma, lymphoma granulomatosum, lymphomatosis granulomatosa,[2] Hodgkin's granulomatous lymphoma,[3] Sternberg's lymphatic glandular disease,[4] granulomatosis textus lymphatici (Typus Paltauf-Sternberg),[5] lymphogranulomatosis (Paltauf-Sternberg),[6] malignant granuloma (granuloma malignum) of the lymphatic apparatus (Benda[7]), malignant granuloma with giant cells,[8] granuloma-like sarcoma of lymphatic glands.[9] The last name fits in best with those cases in which, on microscopic examination after death, the granulomatous growth is found to

[2] Fraenkel and H. Much, Zeitsch. f. Hygiene, Leipzig, 1911, lxvii, 159; see also Münch. med. Woch., 1910, lvii, 685.

[3] D. Symmers, Publications of Cornell Univ. Med. College: Studies from the Depart. of Path., 1909, vol. ix (separate pagination).

[4] J. Sailer, Philadelphia Med. Jour., 1902, ix, 615, 669; A. Sticker and E. Löwenstein, Centralbl. f. Bacteriol. etc., 1910, lv, 267.

[5] H. Lehndorff, Jahrb. f. Kinderheilkunde, 1908, lxvii, 430.

[6] E. Fabian, Wien. klin. Woch., 1910, xxiii, 1515, and Centralbl. f. allg. Path. u. path. Anat., Jena, 1911, xxii, 145.

[7] Verhandl. d. Deut. pathol. Gesellschaft, Jena, 1904, i, 123.

[8] Schwenkenbecher and Fischer, Abstract in Münch. med. Woch., 1911, lviii, 220.

[9] Dietrich, Deut. med. Woch., 1908, xxxiv, 1188.

have invaded bloodvessels,[10] as it did in the case of a man, E. F., aged twenty-seven years, who was under my care in 1905, and whose case I have elsewhere[11] described. Bone erosion from pressure in Hodgkin's disease[12] might clinically suggest a still greater degree of malignancy. The term pseudoleukemia, which has been widely employed in Germany as synonymous with Hodgkin's disease, is said to have been first introduced in 1865 by J. Cohnheim,[13] but it was apparently not intended by him as synonomous with Hodgkin's disease.[14] If the term pseudoleukemia is to be retained in medical literature, it should probably be reserved for those cases of so-called lymphosarcomatous, or, better, lymphocytomatous, infiltration of the kidneys, intestines, or other parts of the body, with small, round lymphocyte-like cells, which separate the cellular elements of the infiltrated part without destroying them, thus giving rise to a microscopic picture, exactly resembling that of lymphocythemic infiltration in lymphocythemia or lymphocytic leukemia, but unaccompanied by any lymphocythemic blood changes.[15]

It is highly probable that some of the supposed cutaneous manifestations of Hodgkin's disease have been really lymphocytic nodules in the skin occurring during an early (aleukemic) stage of leukemia. In some cases of Hodgkin's disease a pruriginous eruption develops, which may even progress to a condition of almost universal erythrodermia exfoliativa. The glandular swellings may then be wrongly supposed to be secondary to the cutaneous eruption.[16] In a case that I saw in private practice the itching was present several months before the glandular enlargement was observed.

There are no blood changes characteristic of Hodgkin's disease, but a polymorphonuclear leukocytosis is fairly often met with,[17] probably sometimes as a reaction toward counterinfections of various kinds. A relative increase of lymphocytes, "sign of Pinkus,"[18] probably more often occurs in the cases of pseudoleukemia (lymphocytomatosis or lymphosarcomatosis) to which I have already referred, and it is, of course, found[19] in early, so-called aleukemic stages of lymphocytic leukemia (lymphocythemia). Leukopenia[20] may occur, as proved by the present case, in late stages of Hodgkin's disease,

[10] Dietrich, Deut. med. Woch., 1908, xxxiv, 1188. Also W. T. Longcope, Bull. Ayer Clin. Lab. of the Pennsylvania Hospital, 1903, No. 1, p. 4; 1906, No. 3, p. 86; 1907, No. 4, p. 18.

[11] F. P. Weber, St. Bartholomew's Hosp. Reports, London, 1908 (for year, 1907), xliii, 81.

[12] W. B. Warrington, Liverpool Medico-Chirurgical Journal, 1911, xxxi, 53.

[13] Virchow's Arch., 1865, xxxiii, 451.

[14] D. Symmers, loc cit.

[15] Fürstenberg and Buchmann, Ziegler's Beiträge z. path. Anat. u. z. allg. Path., 1907, xlii, 447. F. W. Higgs, Proc. Roy. Soc. Med. (Children's Section), 1909, iii, 17. Sterling, quoted by Werdt, vide infra. F. P. Weber, Trans. Path. Soc., London, 1896, xlvii, 117, and Trans. Med. Soc., London, 1909, xxxii, 100, 101. H. Wehland, quoted by Werdt, vide infra. F. von Werdt, Frankfürter Zeitschr. f. Path., 1909, ii, 616; also Banti, quoted by Werdt, loc. cit.

[16] H. D. Rolleston, Brit. Med. Jour., 1909, ii, 852.

[17] E. Fabian, loc cit.

[18] E. Fabian, Deut. med. Woch., 1910, xxxvi, 261.

[19] F. P. Weber, loc. cit., see 11.

[20] E. Fabian, loc. cit.

when extensive fibrosis and necrotic changes have taken place in the spleen and lymphatic glandular apparatus of the whole body. Leukopenia must certainly not be regarded as a pathognomonic sign of splenic anemia or Banti's disease, if, indeed, splenic anemia can be regarded as anything more than a symptom complex, due to various causes, and Banti's disease as a late stage of that symptom complex characterized by the presence of cirrhosis of the liver with or without ascites. But to this question I shall return later.

Since Carl Sternberg's well-known paper (1898),[21] "On a peculiar Form of Tuberculosis of the Lymphatic Apparatus Presenting the Clinical Features of Pseudoleukemia," it has been generally acknowledged (1) that cases of tuberculous disease of lymphatic glands are not very rarely met with clinically, resembling Hodgkin's disease; (2) that tuberculosis occasionally occurs as a superadded infection in cases of Hodgkin's disease. In spite of Musser's[22] and Sailer's[23] summing up, I think that the work of Andrewes,[24] Reed,[25] Simmons,[26] Longcope,[27] Warnecke,[28] Muir,[29] Kidd and Turnbull,[30] and other writers abundantly proves the existence of Hodgkin's disease as a distinct disease or group of diseases with a characteristic morbid histology of its own, although the clinical and postmortem features may sometimes be masked by associated tuberculosis. I have elsewhere[31] discussed this association of Hodgkin's disease with tuberculosis, but I shall here shortly describe another striking example of such association.

The patient, Max L., aged forty-four years, was admitted under my care at the German Hospital on April 22, 1908, and the history of enlarged lymph glands dated from early in 1902. On admission, the spleen and liver could both be felt below the ribs, and there was much enlargement of the lymphatic glands in the neck, armpits, and groins. There were walnut-sized glandular clumps in the axillæ and considerably larger swellings in both inguinal regions, especially on the left side.

There was some ascites. A blood examination by Dr. Chapuis gave: Hemoglobin, 45 per cent.; red cells, 2,500,000 in the cubic millimeter; color index, 0.9. The white cells, especially the polymorphonuclear leukocytes, were greatly increased in number. Treatment by Röntgen rays, which had been previously tried elsewhere, atoxyl, etc., did no permanent good. The patient's general condition varied from time to time, and there were occasional

[21] Zeitschr. f. Heilkunde, 1898, xix, 21.
[22] Trans. Assoc. Amer. Phys., 1901, xvi, 638.
[23] J. Sailer, loc. cit.
[24] Trans. Path. Soc., London, 1902, liii, 305.
[25] Johns Hopkins Hosp. Reports, 1902, x, 133.
[26] Jour. Med. Research, 1903, ix, 378.
[27] W. T. Longcope, loc. cit.
[28] Mitteil. a. d. Grenzgebiet. d. Med. u. Chir., Jena, 1905, xiv, 275.
[29] Glasgow Med. Jour., 1905, lxiv, 161.
[30] Arch. Path. Inst., London Hospital, 1908, ii, 130 to 155.
[31] F. P. Weber, loc. cit., sec. 11; Lancet, London, 1904, i, 924 to 928. (Contains references to older literature on the relation of tuberculosis to Hodgkin's disease.)

periods of pyrexia. In June, 1908, there was still a large polymorphonuclear leukocytosis present; the white cells numbered 18,550 in the cubic millimeter of blood. A right-sided pleuritic effusion needed occasional tapping in September and October, 1908. In November, 1908, some diminution was noted in the size of the lymphatic glands in the right groin. There was still much leukocytosis, 28,000 white cells in the cubic millimeter of blood. In 1909 the patient suffered from increasing feebleness, emaciation, and dropsy, and died on February 21, 1909. At the postmortem examination and subsequent microscopic examination tuberculous lesions were found in the lungs, liver, spleen, and lymphatic glands, and a necrotic change, probably of tuberculous origin, was present in one of some whitish nodules from the bone marrow, which was red in color, of the shaft of the left humerus. But in the largest inguinal gland, kindly examined by Dr. J. C. G. Ledingham, the characteristic features of Hodgkin's disease were detected. It is by the way, perhaps, worth mentioning, that Calmette's ophthalmoreaction for tuberculosis had been tried in May, 1908, with a negative result.

The necrotic and lardaceous changes found after death in the viscera of some cases of Hodgkin's disease, as in the case of H. A., specially under consideration, by their resemblance to changes found in cases of syphilis, tuberculosis, and other microbic diseases, suggest that the exciting cause of Hodgkin's disease is a microbic infection of some kind. Similarly, the fibrotic and cicatricial changes which form so conspicuous a feature in the pathological histology of late cases of Hodgkin's disease are probably analogous to the conservative and limiting fibrosis of chronic tuberculous and tertiary syphilitic lesions. The microbic theory is likewise supported by the occasional occurrence of very acute cases, to examples of which I have elsewhere[32] drawn attention. Acute cases have also quite recently been described by A. T. Wilkinson,[33] J. Mitchell Clarke,[34] and Hirschfeld and Isaac.[35] But though the cause of Hodgkin's disease is almost certainly microbic, attempts at inoculation and cultivation have repeatedly given negative results. Pröscher and White,[36] indeed, in 1907, reported that, by the Levaditi and Giemsa methods of staining, they had succeeded in detecting spirochetes of some kind in human lymphadenomatous glands, but their results have not been confirmed by other investigators. Neither is the recent paper by Eug. Fraenkel and H. Much,[37] of Hamburg, very convincing. These observers claim that Hodgkin's disease, which they call lymphomatosis granulomatosa, is produced by granule-like

[32] F. P. Weber, loc. cit., see 11.
[33] Manchester Path. Soc., March 10, 1909; also Lancet, 1909, i, 920.
[34] Jour. of Path. and Bact., Cambridge, 1908, xiii, 92.
[35] Med. Klinik, 1907, iii, 1580.
[36] Jour. Amer. Med. Assoc., 1907, xlix, 774, 1115; also Münch. med. Woch., 1907, liv, 1868.
[37] Loc. cit.

bacteria (granules of Much), which are intimately allied to, if not actually a variety of, the Bacillus tuberculosis, and which are said to be stained by an intensified Gram method, and though not "acid-fast," to be resistant to antiformin. Here, I may mention that Sticker and Löwenstein,[38] who think that Hodgkin's disease is probably caused by bovine tubercle bacilli, claim that, by inoculation of material from cases of Hodgkin's disease in man, they have succeeded in producing a granulomatous tissue in guinea-pigs, which, although apparently free from tubercles and tubercle bacilli, nevertheless is capable of setting up obvious tuberculosis when it is reinoculated into other guinea-pigs. Obviously such results need much confirmation before acceptance.

In true Hodgkin's disease the lymphatic glands of some one region of the body are much more enlarged at first than the others, as if they constituted the primary focus or centre of the disease.[39] Not rarely, as in the present case of H. A., those on one side of the neck are chiefly affected at first; sometimes a group of retroperitoneal glands seems to be primarily involved;[40] in a case under my care in 1908 the disease commenced in the mediastinum,[41] and so it did in a boy, aged four years, whose case is one of those described by Kidd and Turnbull;[42] Douglas Symmers[43] has described a case which he regards as one of "primary Hodgkin's disease of the spleen." However, Symmers' case is by no means conclusive. The patient, a woman, aged eighteen years, died on the day following the operation of splenectomy, and the spleen was examined microscopically, but no postmortem examination of the other abdominal and thoracic contents was obtained. I believe that the disease, when it is localized in the mediastinum, as it was in a case of mine, to which I have just referred,[44] may give rise to a regular tumor-mass, not merely a conglomeration of lymphatic glands.

In the present cases (H. A.), as doubtless in several other cases, the superficial lymphatic glands, which at first formed a prominent tumor on one side of the neck, shrivelled up during the course of the disease so as to become hardly noticeable. The disease superficially appeared to be in process of cure, but in reality, the lymphatic glands in the thoracic and abdominal cavities and the lymphatic tissue of the spleen were becoming gravely affected. Something of the same kind is doubtless what happens in many cases in which more or less complete cure is supposed to have been affected by arsenical medication or by the action of Röntgen rays. As the disease progresses, the lesions of Hodgkin's disease tend to become more and more fibrotic and to lose their characteristic microscopic

[38] Loc. cit.
[39] F. P. Weber, loc. cit., see 11.
[40] W. T. Longcope, loc. cit. F. Warnecke, loc. cit.
[41] F. P. Weber and J. C. G. Ledingham, Proc. Roy. Soc. Med. (Clinical Section), 1909, ii, 66.
[42] Loc. cit.
[43] Loc. cit.
[44] Weber and Ledingham, loc. cit.

features. This is well illustrated by the present case (H. A.), and by one or two unpublished cases of which Dr. Ledingham has told me. Probably in most cases a counterinfection of some kind takes place at the end, and in the case of H. A. the presence of streptococci in the perivascular lymph spaces of lymphatic glands affords evidence of such a terminal infection.

With regard to clinical diagnosis in the present case, the negative results of Wassermann's seroreaction for syphilis and von Pirquet's cutireaction for tuberculosis were of some value, and leukemia was completely negatived by the blood picture. Hodgkin's disease may perhaps be simulated[45] by malignant disease of abdominal viscera (suprarenals) with secondary infiltration of lymphatic glands in the neck, but had there been any such abdominal malignant disease in the present case, one would have expected enlargement of the inguinal as well as of the cervical glands to have ultimately occurred; moreover, the diminution and almost complete disappearance of the cervical swelling would hardly have been likely, had it been due to carcinomatous infiltration. H. D. Rolleston[46] and others draw attention to the possibility of cases with splenic enlargement and pyrexia, suggesting a diagnosis of malaria or enteric fever, and, indeed, in the present case it was thought advisable to try Widal's reaction, but the result was negative.

In only a few cases of Hodgkin's disease does the patient's temperature chart help at all in the diagnosis. When there is any fever, it is mostly of an irregular kind with a moderate evening rise, but occasionally a long, regularly recurrent, periodic type of fever[47] is met with, the chronic relapsing pyrexia of Hodgkin's disease, which has been called the "Pel-Ebstein symptom," owing to the writings of Pel[48] and Ebstein,[49] in 1887. Of this, perhaps the most remarkable example in existence is an eight month's chart, recently recorded by C. H. Melland.[50] Such cases have even been labelled "Ebstein's disease." Less regular recurrent "pyrexial crises" are of rather commoner occurrence. During the pyrexial periods the superficial lymphatic glands are sometimes observed to swell, but they occasionally seem to diminish rather than increase in size, as in the case of Hodgkin's disease shown by Dr. J. Porter Parkinson before the Medical Society of London on March 27, 1911.

Wherever possible, the diagnosis of Hodgkin's disease should be confirmed at an early stage of the excision and microscopic examination of one of the enlarged lymph glands. Without the help of a biopsy it is by no means always so easy, as some probably suppose,

[45] H. D. Rolleston, personal communication. [46] Practitioner, 1911, lxxxvi, 496.
[47] F. de H Hall, Practitioner, 1911, lxxxvi, 473. L. Hofbauer, Wien. med. Woch., 1905, lv, 86. J. H. Musser, loc. cit. F. Taylor, Guy's Hosp. Reports, 1906, lx, 1.
[48] Berliner klin. Woch., 1887, xxiv, 644. [49] Ibid., 565.
[50] Edinburgh Med. Jour., 1911, New Series, vi, 156 to 164, Chart I.

to distinguish Hodgkin's disease from chronic tuberculous or syphilitic enlargement of lymph glands. Many persons are doubtless alive and well today who would have been long since dead had the diagnosis of Hodgkin's disease pronounced on them been the correct one. Mistaken diagnoses in syphilitic and, especially, tuberculous cases doubtless account for many of the supposed cures of Hodgkin's disease. But that arsenical therapy (Fowler's solution, arsacetin, etc.) and the application of Röntgen rays can be of real use in many genuine cases of Hodgkin's disease there can scarcely be a doubt, even if a permanent cure cannot be effected. This consideration makes it very important that the diagnosis should be made as certain as possible by the help of a biopsy, so that arsenical medication may be carefully and methodically pushed, and *x*-rays perhaps also made use of. Mistakes in diagnosis in regard to the question of Hodgkin's disease have, however, sometimes, it must be admitted, been made, even after a biopsy and all other available methods. I may here mention that the great difference in regard to the ordinary progress of the disease between tuberculous lymph glands and the lymph glands of Hodgkin's disease furnishes another argument against the view that Hodgkin's disease is caused by any variety of the bacillus tuberculosis.[51]

A point of extreme clinical interest in the present case was the development of splenic enlargement and ascites, which, together with the subsidence and practical disappearance of the superficial lymphatic glandular tumors and the association of marked leukopenia with the anemia, produced the clinical picture of Banti's disease, that is to say, the stage of splenic anemia characterized by hepatic cirrhosis and ascites. So great, indeed, was the clinical resemblance, that the diagnosis of Banti's disease was actually arrived at by medical men who had not had an opportunity of seeing the case at an earlier period when the superficial glandular swelling in the neck was the most marked feature. The leukopenia may have been a result of the fibrotic and necrotic changes which involved so large a proportion of the lymphadenoid apparatus of the body.

Granting that there is a definite disease which may be termed splenic anemia, or, in its later stages, Banti's disease, I will now shortly consider a few of the conditions which may clinically simulate it.

Remarks on Various Cases Presenting the Clinical Picture of Splenic Anemia (Banti's Disease). Hodgkin's disease, or lymphadenoma, "with splenic predominance," as seen in the late stages of H. A., the present case, that is to say, a kind of splenic type of Hodgkin's disease, has been likewise called the Griesinger or

[51] Fraenkel and Much, loc. cit. J. H. Musser, loc. cit. J. Sailer, loc. cit. G. Sternberg, loc. cit. Sticker and Löwenstein, loc. cit.

lymphadenomatous type of splenic anemia, but Griesinger's original case, described by his pupil, Gretsel,[52] in 1866, was apparently not a certain one. The patient was a female child, aged only ten months, with great enlargement of the spleen and less enlargement of the liver, moderate rickets, and no leukemic blood changes. At the necropsy the lymphatic glands of the mesentery and retroperitoneal region were found enlarged, and Cohnheim, who examined the spleen microscopically, reported that it showed only hyperplasia of its normal constituents. There was a kind of fibrosis in the liver and kidneys. Griesinger's case cannot, therefore, with certainty be claimed as one of Hodgkin's disease in the modern sense of the term.

Leukopenia occurs in various conditions other than splenic anemia, conditions in which the spleen is chronically enlarged and has undergone extensive fibrotic or necrotic changes, and in which probably a great portion of the total lymphadenoid apparatus of the body is involved. I have already referred to the occurrence of leukopenia in the later stages of Hodgkin's disease. Leukopenia may occur in chronic malarial and syphilitic[53] disease of the spleen and liver.[54] Thus, S. S. Cohen and Rosenberger[55] drew attention to the occurrence of blood changes resembling those of Banti's disease in a case of splenomegaly apparently due to malaria. The connection of some cases of supposed Banti's disease with congenital or acquired syphilis has been suggested by Marchand[56] and others.[57]

Among hospital patients occasionally met with in London are sailors and various persons who give a history of having had malaria and having repeatedly visited or resided in hot climates, and who suffer from anemia with chronic splenomegaly, enlargement of the liver, doubtless a form of hypertrophic cirrhosis, and sometimes marked leukopenia.

In a man, M. C., aged twenty-five years, who had spent twelve years of his life in Jerusalem, where he had suffered a good deal from malaria, there was much enlargement of the spleen and considerable enlargement of the liver, slight jaundice, and anemia. While he was under my care at the German Hospital the number of his white corpuscles varied from 1200 to 4200 in the cubic millimeter of blood. His general health and appearance improved markedly and the jaundice disappeared.

A soldier, W. V., aged twenty-six years, was under my observa-

[52] Berl. klin. Woch., 1866, iii, 212.

[53] Leukopenia may likewise occur in splenomegaly due to primary tuberculosis of the spleen. In such a case described by P. Albrecht at a Viennese Medical Society (Wiener med. Woch., 1908, lviii, 2854) the white cells were counted at 3000 in the cubic millimeter of blood before the operation of splenectomy.

[54] L. d'Amato, Zeit. f. klin. Med., Berlin, 1905, lvii, 261.

[55] Amer. Jour. Med. Sci., Philadelphia, 1904, cxxviii, 271.

[56] Münch. med. Woch., 1903, l, 463.

[57] W. Schmidt, Münch. med. Woch., 1911, lviii, 625.

tion, in 1903, for enlargement of the spleen and liver, emaciation, anemia, slight albuminuria, and oozing of blood from the gums. He had lived for six years in India, where he had had attacks of enteric fever and malaria. He had been accustomed to a good deal of alcohol. When I saw him no malarial parasites were found in the blood and there was no leukemia. His white corpuscles varied between 3748 and 7180 in the cubic millimeter of blood. I heard that he died of "syncope" in September, 1903, and that there was a postmortem examination, but I could ascertain little more than that the spleen weighed 6½ pounds, the liver 10 pounds, and the heart 15 ounces.

In apparently similar cases the pathology and etiology may sometimes be very complicated. An example of this is the case of W. S., a fireman on a steamship, aged forty-two years, whom I showed to the Medical Society of London on April 8, 1907.[58] He gave a history of having taken a good deal of alcohol, of having contracted a chancre ten years ago, and of having suffered from fever, apparently malaria. He was anemic and the size of his spleen and liver was enormous. When at the German Hospital, in London, his white corpuscle count varied from 4160 to 10,000 in the cubic millimeter of blood. No malarial parasites were found, and some blood films from the liver were kindly examined by Captain W. G. Liston, I.M.S., for kala-azar parasites,[59] but with negative result. The patient afterwards went to a hospital at Stockholm, where he had to be tapped for ascites. A blood count made at Stockholm gave: Red cells, 3,500,000 in the cubic millimeter; white cells, 4300 in the cubic millimeter; polymorphonuclears, 70 per cent.; large lymphocytes, 16 per cent.; small lymphocytes, 12 per cent.; eosinophiles, 2 per cent.; hemoglobin, by von Fleischl's method, 50 per cent. He died in the hospital on May 19, 1908, and the Medical Superintendent, Dr. G. D. Wilkens, who very kindly wrote to me about the case, summed up the changes found at the postmortem examinations as follows: Fibrous pericarditis, with complete adhesion of the two surfaces; chronic fibrous myocarditis; acute pneumonia of the lower lobe of the right lung; hepatic cirrhosis; splenomegaly with fibrous induration and spots of pigmentation, possibly left by old malaria; tuberculous peritonitis; tuberculosis of the bronchial and periportal lymphatic glands.

A very interesting case of chronic malignant endocarditis simulating splenic anemia[60] came under my notice in 1909. The patient, G. W., was a sailor, aged twenty-eight years, who had contracted

[58] F. P. Weber, Trans. Med. Soc., London, 1907, xxx, 393.

[59] Cf. cases of hepatic cirrhosis due to the protozoal parasite of kala-azar, described by L. Rogers (Ann. Trop. Med. and Parasitol., Liverpool, 1908, ii, 147); also the cases of infantile splenomegaly with anemia, due to Leishman parasites, described by Nicolle, Jemma, Pianese, Gabbi, Feletti, Cannata, and others.

[60] F. P. Weber, Trans. Med. Soc., London, 1910, xxxiii, 83.

malaria in the Straits Settlements about four years previously. When seen in London, however, he presented no signs of active malaria, and had already been treated at several London hospitals, where apparently the diagnosis of splenic anemia had been made. At the German Hospital he was extremely pale, weak, and wasted, and there was a tendency to bleeding from the gums. His spleen extended downward into the inguinal region, and his liver was likewise enlarged and hard. His legs were pigmented as a result of a chronic petechial eruption, and there were a few minute hemorrhages in the skin of the arms and trunk, in the conjunctivæ, and in the retinæ. There was great anemia with leukopenia. Red cells, 1,700,000 in the cubic millimeter of blood; white cells, 1200 to 1900 in the cubic millimeter; hemoglobin, 30 to 35 per cent. The heart was somewhat enlarged and there was a systolic apical murmur. The necropsy showed the presence of chronic malignant endocarditis, and a microscopic examination by Dr. J. C. G. Ledingham of pieces of the spleen, liver, kidney, and bone marrow from the shaft of the humerus, showed, in all four organs, as their most conspicuous pathological histological feature, a plasma cell development with the elaboration of new fibroblastic tissue.

Perhaps, after all, in the present state of our knowledge, splenic anemia, with its later stage, known as Banti's disease, is best looked upon as a symptom group, which may be set up by various pathogenic agencies, the nature of some of which is known, though that of others has not yet been discovered.

In quite a considerable number of cases presenting during life the clinical features of splenic anemia, old thrombotic obstruction of the splenic and portal veins, with sometimes more extensive recent thrombosis as well, has been discovered after death. For examples of that kind we could refer to the published cases of Dock and Warthin,[61] 1904, Oettinger and Fiessinger,[62] 1907, Edens,[63] 1907, F. Dévé,[64] 1908, and several others; occasionally the splenic artery has been found diseased. In some of these cases the splenomegaly was doubtless secondary to the obstruction in the splenic and portal veins, but in other cases the vascular disease may have been secondary to a toxemia of splenic origin.

Cases of biliary cirrhosis of the liver, Hanot's type, with splenomegaly,[65] are, owing to the chronic jaundice, seldom likely to be diagnosticated as cases of splenic anemia. The Gaucher type of primary splenomegaly[66] is scarcely ever met with. But there are certain cases of congenital or acquired chronic acholuric, so-called

[61] Amer. Jour. Med. Sci., Philadelphia, 1904, cxxvii, 24.
[62] Revue de Méd., Paris, 1907, xxvii, 1109.
[63] Mitteil. a. d. Grenzgebieten d. Med. u. Chir., Jena, 1907, xviii, 59.
[64] Normandie Médicale, March 1, 1908; abstract in Arch. des Maladies du Cœur, etc., Paris 1908, i, 606.
[65] F. P. Weber, Trans. Path. Soc., London, 1903, liv, 103.
[66] Weber and Dorner, vide infra.

hemolytic jaundice, with splenomegaly and anemia,[67] which might, owing to the temporary or permanent absence of obvious clinical jaundice, be mistakenly labelled as examples of splenic anemia. Such cases might be headed splenomegalic anemia or splenomegalic hemolytic anemia, acquired or congenital, to avoid the confusion with splenic anemia.[68] In a paper,[69] with Dr. Dorner on "Four Cases of Congenital Acholuric Jaundice in One Family," we wrote: "It is highly probable that in some cases of the disease the jaundice, at all events, obvious jaundice, may be intermittent instead of remittent, that is, that for a time at least jaundice may be apparently absent, though the splenomegaly and characteristic blood features of the disease are present. Such cases might be clinically termed cases of splenomegalic anemia. . . . In other words, it appears almost certain that a form of splenomegalic anemia without jaundice may occur, although, perhaps, only temporarily, as an incomplete form of the chronic splenomegalic acholuric jaundice, of which the family in question affords complete examples."

In conclusion, I must specially thank Dr. Daser for his information on the early history of the patient H. A., Dr. Dorner for his help in the examination of the same case at the German Hospital, and Dr. Ledingham for his kind report on its pathological histology.

THE INSIDIOUS ONSET OF PNEUMOTHORAX.[1]

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It is unnecessary to attempt to enter here into a detailed description of pneumothorax, its etiology, symptoms, or treatment. This condition is so well known nowadays, and its recognition, despite its protean symptomatology, so well established by the enormous amount of work and the multitudinous articles on this subject, that anything further seems superfluous. There is, however, a certain type of case in which pneumothorax seems to be quite frequently overlooked. I refer to those instances in which the pneumothorax develops insidiously, without the classical signs of sudden pain and intense dyspnea. A pneumothorax developing

[67] F. P. Weber, Amer. Jour. Med. Sci., Philadelphia, 1909, cxxxviii, 24; F. P. Weber and G. Dorner, Lancet, London, 1910, i, 227.

[68] Armand-Delille, Soc. de Pédiatrie, Paris, June 23, 1910. Armand-Delille and Feuillée, Soc. méd. des Hôpitaux de Paris, February 2, 1909. Chauffard and Troisier, Soc. Méd. des Hôpitaux de Paris, February 19, 1909. R. Hutchison, Case of Splenomegaly, shown at the Clinical Section of the Royal Society of Medicine, March 10, 1911.

[69] Weber and Dorner, loc. cit.

[1] Read before the Section on General Medicine of the College of Physicians, April 24, 1911.

slowly or silently without symptoms tends to escape notice, and especially if it occurs in an apparently healthy individual, or, less excusably, in the presence of active pulmonary tuberculosis, the signs of which may obscure the findings. Furthermore, the very type of pneumothorax which is most difficult to detect is also most liable to develop insidiously. It is obvious that a small circumscribed partial pneumothorax will not only give less clear physical signs, but also fewer symptoms. It is the insidious development of pneumothorax that I wish especially to emphasize, and I have chosen such cases to report as I hope will illustrate this.

The first case to be reported is from Dr. Alfred Stengel's service at the University Hospital:

CASE I.—M. R., white, male, aged twenty-three years, car conductor, was admitted on December 1, 1903 with the following history: Present illness began last winter, with a "heavy cold" in chest. Patient had only cough and general weakness, but was compelled to give up work at intervals of a few days or weeks, until about three months ago, when he had to give up entirely. He had slight pain in chest at times, but it was not a prominent symptom. Dyspnea had been the worst symptom for about three months. He had lost about twenty pounds in weight since last winter. At times he expectorates large amounts of sputum, but usually very little. In the summer of 1903 he had on several occasions hemoptysis, at times quite profuse and again slight.

On admission his complaints were cough, weakness, pains in left chest, and dyspnea. Temperature, 99°; pulse, 105; respirations, 26. The physical examination of his thorax is recorded as follows: "Left shoulder carried higher than the right. Chest seems flattened. Left side seems larger than right, and measurement shows a difference of nearly 1 inch, the right measuring 16½ inches and the left 17½ inches just above the nipples. Expansion greater on right; the left side expands very slightly, if at all. No fremitus on left side. There is a tympanitic note over the upper part of the left thorax; anteriorly, flatness begins at the fourth rib, posteriorly at the third spine. The dulness is movable. On the right the lower border of resonance is at the sixth rib anteriorly, and posteriorly at the eleventh spine. No breath sounds heard on the left side; on the right side the breath sounds are puerile. All the signs of pneumothorax are present on the left side. The heart: The apex beat is palpable in fifth interspace, just about ¾ inch inside right nipple line. A pulsation is visible in the third, fourth, and fifth interspaces on the right side. The heart border is inseparable from flatness of fluid on the left side. The cardiac sounds are loud, and there are no murmurs. The remainder of the physical examination was of no importance. The laboratory examinations showed a moderate leukocytosis, but never revealed the presence of any tubercle bacilli on repeated examinations. The future course of the case showed

little change, save that the fluid continued to increase until the pneumothorax was almost replaced by it; finally, a thoracentesis was performed, with the evacuation of forty-two ounces of thick grayish fluid, which produced tuberculosis when injected into guinea-pigs. The patient eventually left the hospital in a much improved condition. Dr. Stengel's last note on the case is as follows: "Points especially worthy of note are: (1) The gradual development of pneumothorax—this method of development I have noted in five out of six cases seen during the past eight months; (2) entire disappearance of the air, with replacement by fluid, speaking for a healing of the rupture, and subsequent absorption of the air; (3) the failure to find tubercle bacilli."

Thus, we have here a case of tuberculosis, as proved by inoculation, with a left-sided pneumothorax developing insidiously, which at first presented the classical signs known as Laennec's pneumothoracic tripod—tympany, absence of fremitus, and absence of breath sounds. As the increasing fluid encroached upward the diagnosis became more difficult, and the possibility of confusing the tympany of the pneumothorax with the skodiac note of a "tympany by mediate relaxation" became greater, this confusion, of course, being decided by the auscultatory phenomena. The displacement of the heart in this case was very great, and its return to a more normal position after thoracentesis very striking.

Another case developing insidiously a pneumothorax in the course of a pulmonary tuberculosis was seen by me in the University Hospital medical dispensary shortly after I had commenced to study this condition, and I am sure that my diagnosis of it was in large measure due to the freshness of the subject in my mind. The diagnosis was agreed in by Dr. R. G. Torrey, and confirmed by skiagraph. The case is as follows:

Case II.—J. W. M., colored, aged thirty-six years, came to the dispensary complaining of cough, pains in chest, and loss of weight. The history of the present illness dated back several months, at which time he developed a cough, which persisted, and two months before we saw him he commenced to lose weight, feel feverish, and have occasional pains in his left chest, and mild dyspnea. No history could be obtained of any sudden attack of pain or dyspnea. The patient was clearly in the last stages of tuberculosis, and examination of his lungs revealed extensive involvement on both sides. In addition, on the left side an area of hyper-resonance was met, which commenced above at the second rib, and extended down, slightly overlapping the heart, and outward to the axilla and the lower part of the posterior aspect up to the tip of the scapula. The note was less hyper-resonant just below the nipple, but in the axilla became loud and booming. Over this area fremitus was almost lost, and the breath sounds were distant bronchovesicular in character. Voice sounds were loud and egophonic in character.

No metallic tinkle or succussion splash could be heard. The stereoscopic skiagraphs taken by Dr. Pancoast show a marked tuberculous involvement of both lungs. The right shows no cavity. The left shows a pneumothorax of the whole lower part of the pleural cavity, being bounded by the heart to the right, above by the second rib anteriorly, and posteriorly extending up to the angle of the scapula. The pneumothorax is crossed in front by a band of adhesions or a marked pleural scar at the level of the fifth rib. These pictures are beautiful, and demonstrate the value of the stereoscopic method, since from neither plate separately could the diagnosis have been made with certainty, but when examined in combination the resulting picture was unmistakable.

The patient was sent to the Rush Hospital under the care of Dr. T. Mellor Tyson, and died there twenty-three days later.

We have here to deal with a partial pneumothorax of tuberculous origin developing insidiously in a case of active tuberculosis. This case is in many respects typical of its kind. Tuberculosis furnishes the vast majority of cases of pneumothorax, and of the stages, it is the active in which this condition is most prevalent. Partial pneumothorax can occur only in such cases as have adhesions already present to prevent its becoming total, and it is in partial pneumothorax that an insidious onset is most frequent. All these conditions were present in this case.

A most exhaustive study of partial pneumothorax has been made by Jaccoud, who classifies them on an anatomical basis, first into superior and inferior, and the inferior again into anterolateral, posterolateral, and of the whole circumference. It is under this latter class that our case should be placed. Of course, the shape, position, and extent of a pneumothorax are entirely dependent on conditions in the pleural cavity, such as adhesions or obliterations.

A third type of case with insidious onset is well illustrated by the following case. I cannot do better than quote verbatim the notes Dr. Stengel gave me concerning this patient:

Case III.—H. La., aged thirty-six years. His previous medical history was uneventful. Was visiting Philadelphia in December, 1903, when he contracted a severe cold, or influenzal bronchitis. His cough was severe, but not productive, and he felt quite depressed and "grippy." He was not conscious of any special oppression, dyspnea, or thoracic pain, and first consulted Dr. Stengel because some of his friends thought he was neglecting a bad cold. Upon physical examination it was found he had partial pneumothorax of the right side. The physical signs—tympany, amphoric breathing, and coin test—were found in the part of the chest midway between the base and apex, and were quite marked. The patient was sent to the University Hospital for rest and care. Within the next twenty-four hours the whole pleural sac became distended with air, and some displacement of the heart toward the left took place.

Soon after this metallic tinkling developed, and after a few days a moderate effusion of liquid was demonstrable. The latter never increased greatly, and at no time rose above the level of the fifth rib in front. Hippocratic succussion was pronounced when the fluid was at its height. The patient was in the University Hospital from December 11, 1903, to January 8, 1904, and was subsequently under observation outside the hospital for another month. During this entire time his temperature was constantly subnormal, and without marked diurnal variations; the pulse rate was never above 90, and much more commonly below than above 80; the respiration rate varied between 20 and 26. After the first few days all cough subsided, and never subsequently recurred. Repeated examinations failed to show any indications of a pulmonary lesion; the superficial glands were not enlarged, and the patient's general nutrition improved steadily from the day he took to bed. The pleural effusion was absorbed within two weeks after its appearance, and soon after this the amphoric breathing ceased, indicating a probable closure of the pulmonary rupture or fistula. This was speedily followed by diminution of the pneumothorax, and within a month by its complete disappearance. The patient was repeatedly examined after his recovery, and no indications of a pulmonary lesion could be detected. He is at this date in perfect health. The most surprising features in this case were the insidious development of a complete pneumothorax, and the absence of marked subjective symptoms affecting either the circulation or respiration, and the absence of discomfort of any sort, which is witnessed to by the patient's utter lack of realization of his condition, and is more remarkable in view of his being himself a well-trained physician. The failure to detect any evidence of tuberculosis of the lungs at the time of the illness and the absence of such during the intervening seven years confirms the diagnosis made at that time of pneumothorax, due to rupture of a superficial air vesicle during a paroxysm of coughing.

These three cases just reported will serve to show the occurrence of pneumothorax, both partial and complete, with insidious onsets under varying conditions. This type of onset is obviously not infrequent, and the large number of cases in which unsuspected pneumothorax is found at autopsy makes it certain that it is quite a common happening. Every author writing on this subject of recent years recognizes both types of onset, and quite a number, among others Emerson,[2] in his monograph, and James,[3] in Osler's *Modern Medicine,* quote the figures of Saussier in his Paris *Theses,* 1841, to the effect that in 196 cases reported there were 68 with sudden onset. At first sight these figures appear remarkable, and

[2] Johns Hopkins Hospital Reports, vol. xi, p. 434.
[3] James, Osler's Modern Medicine, vol. iii, p. 875.

it would be discouraging for us to have to believe that seventy years ago clinicians were recognizing three times as many insidious pneumothoraces as of those developing suddenly. However, Emerson, in the same monograph, several times speaks of Saussier as having been able to collect only 169 cases, and this suggested a possible error. A glance at the original thesis showed the trouble. On page 6 Saussier says: "Les observations sur les quelles mes recherches sont appuyées se montent a 169 et ont été recuillies à une foule de sources;" and later, on page 68: "Les symptomes du pneumothorax ou de la perforation ont paru subitement ou d'une manier lente dans 196 cas ou on a pris la peine de les indiquer, savior: 68 fois d'une subsite et 28 fois d'une manier lente." It is an apparent typographical error, which turns 96 into 196.

Thus, instead of his figures showing a sudden onset in 68 out of 196 cases, they really show a sudden onset in 68 out of 96, or in more than two-thirds of the cases. There is no question that this is the proper interpretation of his figures, since the sum of 68 and 28 is 96; and since having been able to collect only 169 cases, he would scarcely say that in the 196 cases in which the trouble was taken to indicate the onset there were 68 sudden and 28 slow.

This unfortunate author has been quoted from generation to generation throughout medical literature in such a way as to precisely reverse his actual findings, and to complete his discomfort, his name in Osler's *Modern Medicine* is misspelled.

It has seemed worth while, therefore, to collect the figures in a series of cases concerning the type of onset. Of course, no statistics on such a point are free from criticism, especially if culled from the literature, for certain factors determine which cases shall be recorded. However, the number of cases obtainable is so large, and certain individual reports are of such considerable numbers, that the figures are surely approximate.

In the literature of pneumothorax there occur several extensive monographs, and of these the most recent and satisfactory is by Emerson, published in 1903. In this work Emerson gives abstracts of some 358 articles on this subject, and I had hoped at first to be able to collect a sufficient series of cases from those abstracts; but this proved to be impossible, as but few of them detailed the histories of the cases reported. I was therefore obliged to refer directly to the original articles in the majority of instances. Over 1500 cases were reviewed, being found in 180 references in the literature from 1841 to the present time. Of these 1500 cases, 500 were found which gave perfectly satisfactory and sufficient histories of the onset. Every doubtful case and every case which had been subjected to trauma or tapping was omitted. With regard to the onset only two groups were made, sudden and insidious, and the cases were found to be divided as follows: 385 sudden and 115 insidious, adding to a total of 500. These figures expressed in percentages give 77 per cent. sudden and 23 per cent. insidious cases.

This percentage does not probably represent the number of cases with insidious onsets for several reasons: (1) Many cases of pneumothorax with insidious onset are not recognized; (2) fewer of the cases with insidious onset are reported, and (3) many cases with a probable insidious onset had to be ignored on account of insufficient history, whereas in no case of sudden onset would the author fail to mention this striking feature. Nevertheless, the statistics are better than none or incorrectly quoted ones.

In looking over the mass of literature on this subject, many interesting points presented themselves; among others, the fact that there is no relative increase in the cases with insidious onset reported of recent years, as might be expected, and that the figures just quoted, representing almost the entire literature, vary but little from Saussier's true figures collected seventy years ago.

Another point which cannot be overlooked is the large number of cases reported in which a pneumothorax followed tapping of the pleural cavity. The early writers did not emphasize this possibility very strongly, and Biach,[4] in 1880, could find only 3 cases with this etiology out of the 918 he studied. More recently, however, several authors have reported larger numbers. Emerson in 1903 mentions 10 cases out of the 49 he reports, and Ayer,[5] out of 72 cases of pneumothorax, finds that 14 surely followed tapping, while 9 additional ones may have been similarly caused. The actual cause of pneumothorax following aspiration is in many cases obscure, and a number of possible explanations have been suggested: (1) Faulty technique, permitting air to enter from outside; (2) wounding of the lung with the needle; (3) negative pressure may cause the rupture of an emphysematous bleb, or hasten the breaking through of a tuberculous cavity, or adhesions may lead to a tear of the visceral pleura; (4) gas may be liberated from the blood to fill the vacuum; (5) local respiration of the tissues. However fanciful some of these may seem, it appears incredible that faulty technique can be responsible for so many cases as are quoted above by Emerson and Ayer from such institutions as the Johns Hopkins Hospital and the Boston City Hospital. It is, of course, possible that the tympanitic note which is found so frequently over the upper part of the lung after aspiration, and which is usually interpreted as a skodaic note due to relaxation, although no perfectly satisfactory explanation has as yet been advanced, may be the cause of confusion in certain of these cases. I have examined the notes of a large series of cases of hydrothorax tapped at the University Hospital, and have found only one sure case of resulting pneumothorax and a few doubtful ones. A final point in this relation is the remarkable absence of intense symptoms in pneumothorax thus produced, probably

[4] Wien. med. Wochenschr., vol. xxx, No. 1, p. 6.

[5] Boston Medical and Surgical Journal, vol. clxiii, No. 13, p. 501.

explained by the fact that the lung on the affected side was already only partially functionating, owing to compression, by the effusion for relief of which the aspiration was performed, and that respiratory compensation had been established.

As a contrast to the third of the cases I have just reported, which was a total pneumothorax developing insidiously in an apparently healthy man, I wish briefly to mention the following, for the use of which I am indebted to my brother, Dr. William Pepper:

CASE IV.—M. G., white, aged twenty-nine years, single, minister, was first seen on December 25, 1905, complaining of dyspnea and pain in the epigastrium. He gave the following history:

"Five days before admission, while smoking a cigar, the first tobacco he had smoked since a boy, he had a sharp, shooting pain about the middle of the sternum, lasting only a second. He stopped smoking, and was perfectly comfortable until the next day. While on a train he had a similar attack of pain, slightly more on the left side of the chest. This lasted for about one hour, during which time, after he left the train, and while walking, he was quite dyspneic. That evening and night he had considerable pain in the epigastrium and along the spine, and also an oppressive sensation over the chest. On Tuesday his bowels became constipated, and the pain increased over the whole abdomen, and continued along the spine. The next day he was quite comfortable until late in the afternoon, when he had a sharp pain over the whole left chest, with cramp-like pains in stomach and bowels. He was very dyspneic. The pain in the back had shifted to the left loin region, and was dull and aching in character; he had not slept the previous night on account of pain and shortness of breath. The pain in the chest had been relieved."

He was in perfect health at the time of this onset.

Physical examination revealed an almost complete pneumothorax of the left side. The signs were very clear; the left chest was fuller, and moved less on respiration than the right; fremitus was absent on the left side, and percussion gave a hyper-resonant note, less marked at the apex. The normal cardiac dulness was lost, being replaced by hyper-resonance; the cardiac dulness was found to the right of the sternum, extending 1½ inches. Over the left side auscultation revealed cavernous breathing, metallic in character, and the voice sounds were also metallic. Metallic tinkling was occasionally heard, and the coin test was positive. In short, the signs of pneumothorax were all present and typical. The presence of cavernous breath sounds, while perhaps not so characteristic of this condition as absolute silence, is frequently seen, and should not be permitted to militate against a diagnosis of pneumothorax. The findings on the right side were normal in every respect.

The patient was only moderately dyspneic, with a normal tem-

perature, a pulse of 128, and respirations of 28 to the minute, which, however, rose suddenly two days after admission to 44, and then ran a varying course between 30 and 40. The patient remained under observation for two months, during which time the signs in the lungs varied greatly. The notes on the case are very full, and it deserves more study than can be given here. Briefly, the signs of pneumothorax gradually disappeared, and after recovering from a complicating bilateral phlebitis of the long saphenous veins the patient was apparently restored to his former good health. The sputum was repeatedly examined, but no tubercle bacilli were found, and no evidence of any tuberculous process in the lungs discovered. The etiology of this peculiar case remains a mystery, as does also that of the previous case. They both belong to that well-recognized group of spontaneous pneumothorax occurring in apparently healthy individuals.

Since it is my desire merely to emphasize the frequency of insidiously developing pneumothoraces, and since the rest of the cases which were found do not add anything to those already quoted, a detailed account of them seems unnecessary here. In conclusion, let me say that if the figures collected and quoted above truly represent the frequency of recognized cases with these two types of onset, we are forced to the admission that a great number of insidiously developing pneumothoraces are escaping notice. This is true even if we rule out those which are clinically unrecognizable, owing to their small size or position. There is no condition which in its symptomatology more closely obeys the laws of physics and the mechanical principles involved in physical diagnosis, and surely this condition should be consistently diagnosticated by careful physical examination without the necessity of having an alarming sudden onset to direct attention to it. In a later paper I shall discuss the occurrence of partial pneumothorax, a form which, as has been said, is particularly liable to escape notice.

It was some months ago that Dr. Alfred Stengel suggested to me that it might be profitable to look up the cases of pneumothorax which had occurred in his service at the University Hospital, and although I have more or less wandered from the original intent, yet I wish gratefully to acknowledge his suggestion and the use of his cases in this paper.

OBSERVATIONS ON SOUND PRODUCTION AND SOUND CONDUCTION ALONG THE RESPIRATORY TRACT.

By Joseph H. Barach, M.D.,

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In a preliminary communication[1] on the transmission of sound by the bony framework of the thorax and by adjoining osseous structures, I called attention to the tubular-like breathing which is to be heard during the respiratory excursion at certain named areas not previously considered.

Up to the present time the chief claim that those observations may have upon our interest is that they are striking examples of the sound conducting ability of the bony framework of the body, particularly the thorax, and as such, will necessarily direct our attention to a more extensive consideration of the relationship between the various auscultatory phenomena, their manner of production, and source of origin.

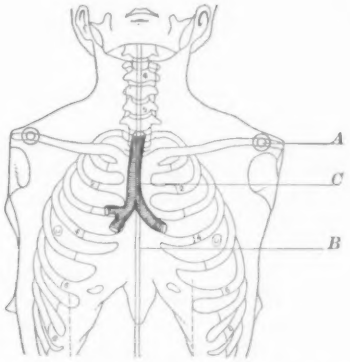

Fig. 1.—*A*, acromion area of bronchial breathing; *B*, median line of the body; *C*, position of the trachea as compared with the median line of the body. (J. C. Blake, Amer. Jour. Med. Sci., 1899.)

My first communication dealt chiefly with the finding of (1) tubular breathing at the acromial end of the clavicle; (2) tubular breathing over the uppermost portion of the spine—this sound I now wish to designate as cavernous breathing (*vide infra*); and (3) cavernous breathing also heard over the occipital and other bones of the cranium (Figs. 1 and 2).

[1] The Role Played in Auscultatory Signs of the Respiratory System by the Sound-conducting Property of the Bony Framework of the Thorax.—Amer. Jour. Med. Sci., December, 1910.

On first hearing this sound one may object to the term "cavernous" as applied here, yet the sound is a true cavernous sound, and such objections are therefore not valid.

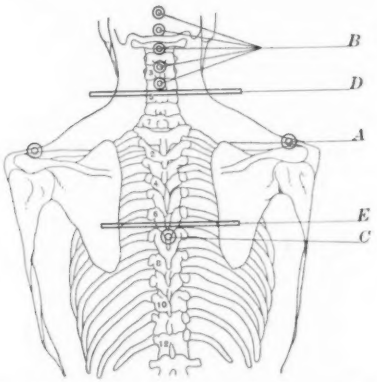

FIG. 2.—*A*, bronchial breathing heard over the acromion area: *B*, cavernous breathing heard above the recognized height; *C*, bronchial breathing heard below the recognized height; *D*, level of the fifth cervical vertebra where bronchial breathing is supposed to end; *E*, level of the fifth dorsal vertebra where the bronchial breathing is supposed to end.

SOURCES OF THESE SOUNDS.

Since up to the present we have only concerned ourselves with respiratory sounds heard from within the thorax proper, and rarely over the trachea, and since the generally accepted theory is that all sound production begins at the larynx, and also finding that bones are such excellent conductors of sound waves, it was a natural inference that the sounds heard at the above-mentioned areas had their beginning in the larynx and trachea.

This was the view accepted at the time of the communication referred to. But further investigations upon the origin and transmission of these auscultatory findings prove that sound production does not begin at the larynx, and that other factors, to be here considered, play a distinct role in determining the quality and quantity of sound heard.

In Fig. 3 I have arbitrarily divided the course of the upper air passage into spaces *A*, *B*, *C*, and *D*, representing the nasal fossa, the oral cavity, the laryngeal space, which includes the larynx and the trachea. Each of these represents an element in sound production and will be here considered.

Space *A*. The nasal fossæ are bounded above by a roof composed of portions of the nasal, frontal, ethmoid, and sphenoid bones and the basilar process of the occipital bone. The floor is formed by

the palatal bones, the outer walls by bones of the face, and the entire space is divided by a bony and cartilaginous septum.

Here we have an irregularly triangular space, bounded by bony walls and divided by a septum. Through this divided chamber passes a volume of air (about 500 c.c.) with each respiratory act, under constant pressure. The friction thus caused along its walls, including the turbinate shelves, necessarily sets up sound vibrations. These vibrations are taken up by the bones which enter into the formation of the walls of this bony cavity, and over some of them the sounds named are to be heard.

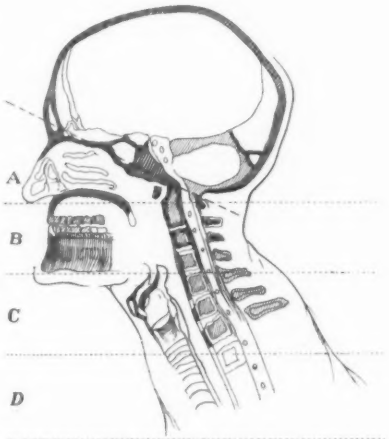

FIG. 3.—Upper air passage divided into the nasal fossa, *A*, the oral cavity, *B*, and the laryngeal and tracheal spaces, *C* and *D*.

Space *B*. The bony elements which may influence the production of sounds under consideration in this space are the teeth, the hard palate, and the posterior wall of the pharynx, which is composed of the cervical vertebræ. A volume of air on inspiration, passing with a definite amount of friction against the teeth, the hard palate, and striking the posterior pharyngeal wall, is certain to create a considerable number of sound waves.

Compared with space *A*, space *B*, as will be shown, plays a less important part in the sound production with which we are here concerned.

Space *C*. In this space lies the important organ of voice production, the larynx. Its cartilaginous walls, their peculiar arrangement, the positions and vibrations of the vocal cords make this organ an important source of sound vibrations, subject, however, within limitations to certain influences.

Space *D*. In this space lies the trachea, which, by virtue of being a cartilaginous and membranous tube, with an interior which has an undulating surface, itself forms an efficient excitor of sound waves. Its large share in sound production also enters into this consideration.

From what has been thus far stated, it is obvious that I regard spaces *A* and *B* of sufficient importance to warrant a consideration of the influence which they have upon auscultatory phenomena of the chest.

CONDITIONS MODIFYING SOUNDS.

Over the occipital area, nasal breathing, mouth closed. By applying the bell of a stethoscope (about the size of the Ford stethoscope) to the occipital bone, below its protuberance, one hears a pure type of cavernous breathing. The expiratory is louder than the inspiratory sound. The reasons for this are, I believe, that the outgoing volume of air strikes the roof of the nasal fossa more directly and more forcibly, and it may also be largely due to the position of the vocal cords, which are closer and vibrate more during expiration.

Mouth Breathing, Nostrils Closed. Without removing the stethoscope, and having the subject open the mouth and at the same time close the nostrils, one will find that the cavernous respiratory sound has almost disappeared.

The reason for this is, that the source of origin of the sound, the nasal fossa as a resonating chamber, has been eliminated. A distant and weaker sound is, however, still heard, and its origin may be from one of two or perhaps from both sources. It may be the faintly transmitted sound from that portion of the spinal column which gets its sound from the larynx, or it may be produced by the moving air in space *B* striking the posterior pharyngeal wall and at the same time setting in motion the residual air in space *A*, creating lesser sound waves and fainter sounds.

Mouth Breathing, Nostrils Open. Having the mouth and nostrils both open gives, on auscultation at the same areas, a louder sound than when the nostrils are closed, but a sound not nearly so large in volume nor high in pitch as when the mouth is closed.

Influence of Nasal and Oral Breathing upon Laryngeal and Tracheal Sounds. Sounds heard when auscultating over the larynx, trachea, manubrium sterni, and acromial ends of the clavicles, are much influenced by opening and closing of the mouth. With nasal breathing, when the nasal fossa acts as a reasonating chamber, the characteristic and familiar "bronchial" breathing is plainly audible. Closing the nostrils and opening of the mouth, thus eliminating the nasal resonator, reduces the volume and pitch of sounds at all of the above-named areas.

Heretofore it has been generally conceded that the production of sound heard over the respiratory organs begins at the larynx. The foregoing observations seem to prove conclusively that a definite amount of sound is created before the larynx is reached. Also that on eliminating the nasal resonating chamber, the various respiratory sounds become weaker, thus showing that the nasal resonator actually does add to the "sound total."

Part Played by the Larynx. During inspiration the downward moving volume of air, carrying with it a certain amount of sound acquired in the nasal resonator, reaches the larynx and there takes up more sound. During expiration, the upward moving volume of air, already charged with sound waves, enters the nasal resonator and there reverberates. So that the column of air which is to enter the larynx at both inspiration and expiration, already is carrying an appreciable amount of sound, and here receives more. How much more, and what actual part the larynx itself plays in the production of auscultatory sounds, I have attempted to determine by studying the physical signs in two tracheotomy cases.[2]

One of these breathed through a tracheotomy tube, and the other through a large tracheal fistula. Here the larynx took no actual part in sound production.

CASE I.—Tracheotomy tube inserted at the second and third cartilages.

Over Cranial Bones. When patient was breathing through the tracheotomy tube only, having closed the nares and mouth, no sounds could be detected at the occipital area, nor anywhere above the level of the tracheotomy tube. Leaving the nose open, which permitted the passage of a limited amount of air through the nasal resonator, was followed by loud cavernous breathing over the entire head and upper portion of spinal column down to the level of the tracheotomy tube. The sounds were almost as distinct over the frontal bone as over the occipital and parietals.

Over Trachea. When the nares were closed and the nasal resonator entirely eliminated, the tracheal sound was softer than when the nares were left open and a small amount of air could pass through the nasal fossa which acted as a resonating chamber.

Over Sternum. At the manubrium sterni, when the patient breathed naturally and air was rushing in through the tracheotomy tube, and some through the nasal fossa, the usual "bronchial" sound was heard. The expiratory and inspiratory sounds were nearly of equal length. Closing of the nares, thus eliminating the nasal resonator, was followed by a weakening of the sounds, of which the expiratory was considerably louder than the inspiratory sound, probably because of backward reflection of sound waves in the trachea resulting from obstruction by the tube.

[2] Through the kindness of Dr. Chevalier Jackson and Dr. Ellen J. Patterson, I was afforded the opportunity of studying these cases.

At the Acromion Areas. With the nares open, and nasal resonator acting, the transmitted bronchial breathing was clearly heard with equal strength on both sides. Closing of the nares made the sound faint and almost inaudible.

In my first communication on this subject I called attention to the fact that the bronchial breathing over the right acromion area was louder than on the left, and also that by auscultating with the median line as a starting point, the tracheal sounds over the manubrium sterni and apices extended to the right side. This observation I have since been able to confirm in the greater number of my examinations, but not in all. Whether in those individuals in whom the acromion sounds are of equal values the trachea is situated nearer the median line, I am at present unable to say.

Right Apex Anteriorly (Bowles' stethoscope). Nose open, vesicular sound quite distinct; nose closed, no sounds.

Left Apex Anteriorly. Nose open, vesicular sound clear; nose closed, sounds very faint, almost inaudible.

Right Apex Posteriorly. Nose open, inspiratory and expiratory sounds audible; nose closed, inspiratory vesicular sound clear, expiratory sound inaudible.

Left Apex Posteriorly. Nose open, inspiratory and expiratory vesicular sounds audible; nose closed, inspiratory vesicular sounds only are heard.

Over Middle of Chest. The characteristic normal vesicular sound is not present. Instead, one hears a rather rough interrupted vesicular type of breathing at some areas, while at others hardly any sound is heard.

At Base of Lungs. On the left side the sounds are better heard than on the right. By using Bowles' resonating stethoscope, when the nares were left open, I could detect both the inspiratory and expiratory sounds. With closure of the nostrils the inspiratory sound alone was audible.

Speech. These patients make attempts at speech by closing of the tracheotomy tube or fistula with their fingers, and during expiration set the vocal cords or remnants of the same into vibration. The resulting sound, which is a kind of a barking whisper, is transmitted by the osseous structures just as clearly as the normal spoken voice.

CASE II.—This patient breathed freely through a large tracheal fistula, the tube having been discarded.

Cranium. At the occipital area cavernous breathing could be heard when the nares were open or closed. In the other case, when the nares and mouth were closed no sounds were audible; the column of air passing through the tracheotomy tube did not reach the nasal resonating chamber. In this case both the inspired and expired air had access to the nasal cavity, and sound was carried.

Acromion Areas. On the right side, when the fistula was closed, bronchial sounds were distinct; when the fistula was open, the sounds were very faint or imperceptible at times. The left side was the same.

Apices Right and Left. When fistula was closed, the respiratory sound was audible. The sound heard corresponded more to a weak and indistinct bronchial sound than a pure vesicular murmur. When the fistula was uncovered, the respiratory sound was very distant and its character doubtful.

Middle and Lower Lobes. The respiratory sounds were atypical. Bronchial breathing at the median line lacked the quality which characterizes it in the normal, and the vesicular murmur seemed to be replaced by a distant and weaker sound. At the bases posteriorly, inspiration was longer than expiration, and was louder, as the normal vesicular murmur should be. In the axillary aspect of the chest there was a short inspiratory sound and no expiratory sound was audible. Thus, the sounds over most of the chest seemed very distant and weak. Tactile fremitus was imperceptible. Vocal resonance could be heard.

The observations in these two cases show that elimination of the larynx does alter the auscultatory findings, but not sufficiently to change their character. They confirm the previous findings that the sound created within the nasal resonating cavity is a part of the "sound total" which presents itself to us for auscultation over the thorax.

Before my conclusion I wish to note that in this consideration I have dealt with the physiological only. It is needless to say that abnormal configurations and pathological conditions of any of the anatomical parts which enter into this sound-producing and sound-conducting system will respectively modify the findings.

By this study I intended leading up to the consideration of sound transmission in the various pathological conditions.

SUMMARY AND DEDUCTIONS.

In calling attention to the auscultatory findings at the specified areas of the thorax and skull, I desired first to set forth prominently, the sound-conducting ability of the osseous system, particularly the thorax. When it is fully appreciated that sounds emanating at one spot can be transmitted to another, the importance of studying auscultatory signs from such a viewpoint becomes apparent.

Thus, I found that the "bronchial breathing" heard at the acromial end of the clavicle has its origin at the manubrium sterni, which receives sound vibrations from the trachea behind. The cavernous breathing heard over the cranial bones, particularly the occipital, has its source of origin in the nasal fossa which acts as a resonator.

In the nasal fossa, the nasal resonator, a definite amount of sound is produced, and this sound added to the sound wave created along the lower portions of the respiratory tract, makes up the "sound total," which is heard when auscultating.

That the nasal resonator is an active factor in auscultatory sound production is readily appreciated by observing the weakening of the respiratory sounds which occurs when its action is eliminated. From this it is evident that auscultatory sound production does not begin at the larynx. This too, shows that the examiner must take into careful consideration the condition of the nasal resonator, and whether the mouth is open or closed, in the proper interpretation of his auscultatory findings.

The observations upon the tracheotomy cases throw light upon the part played by the larynx, which seems to be of less importance than is generally believed. They show that elimination of the larynx results in modification of the pitch and volume of the bronchial and vesicular sounds, but the essential characteristics of these sounds remain unchanged.

SOME GENERAL CONSIDERATIONS AS TO VISCERAL PTOSIS.

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A ptosis consists, essentially, in a gravitation of an organ, due to some weakness in its normal support. Originally applied mainly to the upper eyelid, and in Dunglison's dictionary of 1874 limited to various ocular conditions, ptosis in recent years has been discussed chiefly as a condition of certain abdominal viscera and, to a less degree, of the heart. While literally applicable to the pelvic generative organs, and properly so, other terms are more commonly employed.

The displacement of an organ outside of the body cavities, to employ a loose expression for an idea which it is difficult to express accurately, is not properly considered as a ptosis. Thus, one does not speak of a ptosis of the thyroid. Obviously, too, the dense, close-fitting walls of the cerebrospinal apparatus prevent the occurrence of this lesion for the corresponding organs.

As stated, ptosis implies a gravitational displacement. Thus, in the perpendicular posture, the displacement is downward and the direction is not necessarily nor, indeed, characteristically altered for other postures. Moreover, the downward displacement is liable to be chronic, and the support of adjoining viscera or of the body wall, more or less regularly for various organs, tends to prevent move-

ments in the horizontal plane, relative to the perpendicular posture of the body as a whole.

A displacement due essentially to encroachment, either of an enlarged organ or of some foreign growth or accumulation, as fluid, etc., or, on the other hand, to traction, as by cicatricial bands, is not essentially a ptosis, even if the displacement is downward, although it is not always practicable to discriminate with regard to the ultimate or complicating causes of displacements of this nature. The definition of ptosis as gravitational, that is, mainly downward in the ordinary vertical posture, must also be qualified to allow for the combination of other forces, as fixed points or planes of resistance, which deflect the organ from a strictly vertical displacement.

Disregarding the female pelvic organs, the conceivable ptoses are as follows: Cardioptosis, pneumoptosis, hepatoptosis, lienoptosis, nephroptosis, gastroptosis, enteroptosis (coloptosis), and more generally splanchnoptosis. The names are purposely given, as some writers substitute mongrel terms for some organs, and the collective ptosis is often designated visceroptosis. These terms cover all of the major organs of the thorax and abdomen. It is hardly conceivable that the suprarenal could be prolapsed without the kidney or the appendix without the cecum, at least.

It is extremely doubtful if the term pneumoptosis, or rather the corresponding conception, is tenable. The lung is a very light, distensible organ, necessarily conforming to the contour of the thoracic wall and floor, and any downward extension of the lung is due to a fault of the diaphragm or of subjacent structures, not to an essential prolapse of the lung itself.

The writer would insist that the term prolapse be limited to a dropping of an entire organ or, at least, of an anatomic unit, as a lobe of the liver or a considerable extent of the colon. Thus, a downward displacement of the heart, not essentially due to a fault of its supports, but to a dilatation, or other form of enlargement, is in no true sense a cardioptosis. This contention will probably not be disputed, indeed, it will more likely be regarded as a truism. It is made in order to support an analogous claim for the stomach. The term gastroptosis frequently occurs in medical literature. Nine times out of ten it applies to the inevitable sagging of the greater curvature of a dilated organ, or, at any rate, it is used without any demonstration that the stomach in its entirety is displaced downward. The term should not be used unless by *x*-ray examination, auscultatory percussion, or some allied method the upper portion of the stomach is also shown to be sagging from its proper level. However, it must be conceded that atonic gastric dilatation, that is, dilatation not due to pyloric obstruction, has many etiologic and pathogenic points in common with gastroptosis.

Hepatoptosis is, in the writer's experience, a very rare condition,

only two cases having been encountered in over a thousand physical examinations, and these in connection with other ptoses. A little consideration, however, will show that the condition is difficult to determine if one starts with the idea not to diagnosticate what cannot be actually demonstrated. In the case of a large liver, which is necessarily heavier than normal, a slight amount of sagging is inevitable and not to be considered a ptosis. Whether by deep ordinary percussion, auscultatory percussion and its modifications, *x*-ray examination, etc., the upper limit of the hepatic area extends higher than normal or not, it is very difficult to judge how much of the depression below the costal arch is enlargement and how much sagging. In the opposite condition, of contraction, the pull of gravity is diminished by the lessened mass of the liver, and the same puzzle, as to distinguishing between the size and relative position of the liver, is present. In actual ptosis the liver tends to rotate on a lateral axis, so as to give the impression of enlargement by physical examination. Then, too, neither with regard to shape, perpendicular diameter, nor relation to ribs, can we lay down exact normal standards for this organ. Finally, there may be mentioned the fact that there is a common tendency to find the liver enlarged or, at any rate, depressed below the costal arch when it is actually of normal size or even contracted. Even men of high standing often fail to realize that when they palpate the edge of the liver so many fingers' breadths below the costal arch, they must subtract the thickness of the abdominal wall which intervenes between their fingers and the liver. The liver may enlarge considerably by mere congestion. For example, the writer has seen the liver retract two inches during a half-hour operation on the gall-bladder, in which considerable blood was lost.

Barring extreme cases, it is doubtful if lienoptosis without enlargement can be diagnosticated. In most cases, the writer can make out by auscultatory percussion a small circular or elliptic area posteriorly, which apparently corresponds to the spleen, although great care must be exercised not to confuse the posterior projection of the gastric area with this. But the area varies so much in apparently normal subjects that it is practically impossible to draw conclusions as to ptosis or even to be absolutely sure that it indicates the spleen at all. The spleen, when considerably enlarged, is usually easily palpable below the ribs, but, as in the case of an enlarged liver, it is difficult to estimate the degree of true ptosis. Marked ptosis of the unenlarged or slightly enlarged spleen is a well-known though rare condition. The differential diagnosis from nephroptosis or other tumors is difficult.

The subject of nephroptosis would fill a volume. As the writer intends to discuss it more fully at a later date, only two points will be alluded to and these merely for the sake of eliciting information and criticism. It is commonly stated that manipulation of a kidney

will often, if not usually, produce albuminuria. This phenomenon the writer has never noted in a series of about 400 to 500 cases, though it should be admitted that a systematic examination of urine for a definite period after manipulation has not been made, nor has the kidney been purposely kneaded. Still, in most cases the urine has been examined within a day after palpation, and in many repeated examinations have been made. Secondly, no instance of a Dietl's crisis has been encountered in this series. In one case a physician reported such an instance, but on visiting the patient, absolutely no history of such an attack could be elicited.

(Uro) Cystoptosis can scarcely exist in the male, except in the sense of an extreme failure of development of bony and ligamentous structures or of the extension of the bladder into a ventral or other hernial sac. In the female partial ptosis is common as a cystocele.

There is no apriori reason why cholecystoptosis should not occur, although, as a matter of fact, the supports of this comparatively small and light organ are not often relaxed to any degree, even when it is weighed down by calculi, distention with bile, or growths. Moreover, at the best, it is not easy to palpate, and perhaps a true ptosis exists more often than it is recognized. It is scarcely necessary to state that the gall-bladder descends with a hepatoptosis.

The term enteroptosis is very commonly employed. Excepting with regard to the transverse colon, it is rather difficult to define this condition. The transverse colon is large enough and has a sufficiently definite location, so that it is usually possible, by a few examinations, to make out a coloptosis. However, there is an extreme and rather rare type of gastroptosis, which may be confused with ptosis of the transverse colon. This type of gastroptosis the writer has termed "banana stomach," from its shape and size. Various methods of intubation, auscultation of air blown through the tube, or of deglutition murmurs, of effervescence produced chemically, *x*-rays, etc., may be used to determine whether the area in question is the stomach.

It is theoretically possible to diagnosticate a typhloptosis by palpation of a low-lying, appendiceal root, perhaps, by vaginal touch, in addition to percussion, auscultation, *x*-rays, etc. Radiography might also be expected to enable the determination of ptosis of the colonic flexures. The sigmoid varies so very widely in length, shape, and position at necropsies that it is difficult to see how ptosis could be defined or diagnosticated with the body wall intact. Excepting in cases of stricture with enormous distention with gas and feces, the writer has not been able to diagnosticate any of these recondite conditions, and in such cases the applicability of the word ptosis is questionable.

Rectal prolapse is, in a sense, a ptosis, but the condition involves also inversion or even intussusception, and should, for practical

purposes, be kept in a separate category. So, too, hernias of all kinds, including diaphragmatic hernias, with descent of the thoracic organs, should be distinguished from true ptoses. In passing, it may be pointed out that neither a diaphragmatic hernia, unless of very rare type, nor the classic illustration of the tongue protruded from the mouth, is a true hernia, the essential definition of hernia including the presence of protruded enclosing membranes.

In a case of intestinal ulceration the surgeon very courteously gave the writer credit for diagnosticating a ptosis of the sigmoid or upper rectum by the use of a speculum. But it is quite beyond the writer's ability even to conceive how a ptosis could be diagnosticated by the use of an instrument which reposits, as it is introduced, and which allows the inspection of only a small circle of bowel at any one time.

By analogy, the more general term enteroptosis would indicate a ptosis of the small intestine. Ptosis of the duodenum, in whole or part, may often be surmised, or, by *x*-ray examination, actually demonstrated, in connection with gastroptosis and hepatoptosis. In one case the writer mapped out, both by *x*-ray and auscultatory percussion, what appeared to be an hour-glass stomach, but which proved to be a moderately dilated stomach, separated by a cancerous pylorus from a considerably dilated duodenum. The latter was somewhat prolapsed. Still, such a case does not answer fully the requirements of ptosis. So, too, as implied in the discussion of the colon, it might be possible to make out an abnormal position of the termination of the ileum. Between these extremes, what anatomy will tell us the normal location of the various sections of the small intestine, or what diagnostician can determine how far such locations are fulfilled?

A number of writers have described at length what they term enteroptosis. Their communications have been, in many instances, detailed and valuable, and, in a literal sense, there has been a sagging of the intestine generally, especially of the small intestine. But the condition that they have described has fulfilled none of the intrinsic requirements of the word ptosis, as established for other organs. There has been a hernial protrusion, a diastasis of the recti, a pot belly, a spinal lordosis, or a long trunk, perhaps with poor musculature. To include such conditions under the term enteroptosis reminds one of President Lincoln's answer to the question as to how long a man's legs should be: "I should say that they ought to be long enough to reach from his body down to the ground." The free intestine, that is to say, all the intestine not bound to the posterior wall of the abdomen, floats in its confines, on itself, in continually changing loops. It permeates all the abdominal cavity, and naturally extends as far as does this cavity, in any direction, either in a general or local protrusion. Unquestionably, thorough, routine postmortem or even operative investi-

gation of a large series might reveal ptoses of individual parts of the small intestine, but at present we have neither anatomic nor diagnostic bases for the use of the word enteroptosis.

Neither should the term enteroptosis be used, as it sometimes is, as a substitute for nephroptosis or a combined ptosis of several viscera. One might just as well say enteritis when he means nephritis or cholecystitis.

Except that the term is more non-committal, the same objection applies to the term splanchnoptosis. There is a general impression that a general splanchnoptosis is quite a common occurrence. Such a conception seems reasonable, and, as ptosis necessarily implies movability, barring secondary fixation, it is obvious that even a total splanchnoptosis would be diagnosticable and would not merely consist of normal relations of viscera at a lower level. The writer has never encountered an instance of total splanchnoptosis and very rarely one involving more than three organs. Extreme abdominal ptoses may occur independently of pelvic prolapses, and vice versa. While slender, neurotic, naturally small-waisted women offer the best material in which to seek for movable kidneys, and while the upright, ptotic stomach is also frequently encountered among them, there is no necessary occurrence of these ptoses, singly or associated. Similarly, broad, flabby, extremely multiparous women, with prolapsed pelvic organs, do not seem to be especially liable to ptoses of other organs, except that the intestine, of course, adapts itself to the pot belly and encroaches more than normally on the pelvic space. However, a word of caution is required in regard to these cases, as the transverse colon and stomach may really sag too low and still be high with reference to the umbilicus.

With regard to the skeletal deformities and muscular atony described as an important factor in "enteroptosis," it should be freely admitted not only that there is a sagging of the intestine following the contour of the abdomen, but that both the lack of anterior and inferior support and the general state of atonicity and malnutrition tend toward genuine ptoses. Still, it is surprising how often these ptoses are lacking.

For these reasons it seems best to discard the term "general splanchnoptosis" except for purposes of classification, and in each case to list the ptoses actually demonstrated.

MULTIPLE METASTATIC ABSCESSES OF THE HEART AND LUNGS IN PYEMIA.

By Robert N. Willson, M.D.,
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The very occasional occurrence of suppurative myocarditis or of circumscribed abscess formation in the cardiac muscle lends to either of these conditions sufficient interest to call for the report and description of each new case. Abscess of the heart is a condition that was known to the ancient physician. It is no more recognizable by clinical signs today than when it was studied on the Egyptian autopsy table. The symptoms and physical signs are those of toxemia, not of a definitely localized suppurative process, and not even of a definite cardiac clinical entity. Yet the possibility of such an occurrence and of such an involvement of the myocardium as was present in the instance described below should ever be borne in mind and have weight in determining both the diagnosis and prognosis in the given case of toxemia.

Beck and Stokes[1] have recently reported an instance of suppurative myocarditis as contrasted with the circumscribed abscess formation seen in cases similar to that here described.

The patient now reported was a trained nurse, aged twenty-four years, serving in the eye ward of the Philadelphia General Hospital. Her family history was entirely negative, both parents being alive and well and one sister a nervous invalid. The patient had never been robust, but was wiry, and always active and energetic. During childhood she had pneumonia; otherwise she had been free from severe illness. One year previous to the history here related she had suffered from a severe and extensive furunculosis, from which she had entirely recovered. Two weeks prior to the present illness, while on duty in the eye ward, a small pimple appeared on the right forehead above the eyebrow. Probably through fingering this pimple infection occurred, and on July 22, 1910, a severe cellulitis and carbuncular suppuration of the scalp followed within a few days. On July 24, 1910, she became quite ill, displayed a temperature of 101° F., and two days later 105° F., and complained of intense pain in the left side. She vomited rather than coughed considerable mucus, and had much nausea. On July 25 the pain seemed to distribute itself more generally throughout the chest, though the original agonizing pain persisted near the apex of the heart and the anterior axillary line. A culture from the scalp pus made by Dr. Randle C. Rosenberger yielded micrococci of suppuration. The right eye at this time became inflamed and discharged a thick pus from

[1] Jour. Amer. Med. Assoc., September 24, 1910.

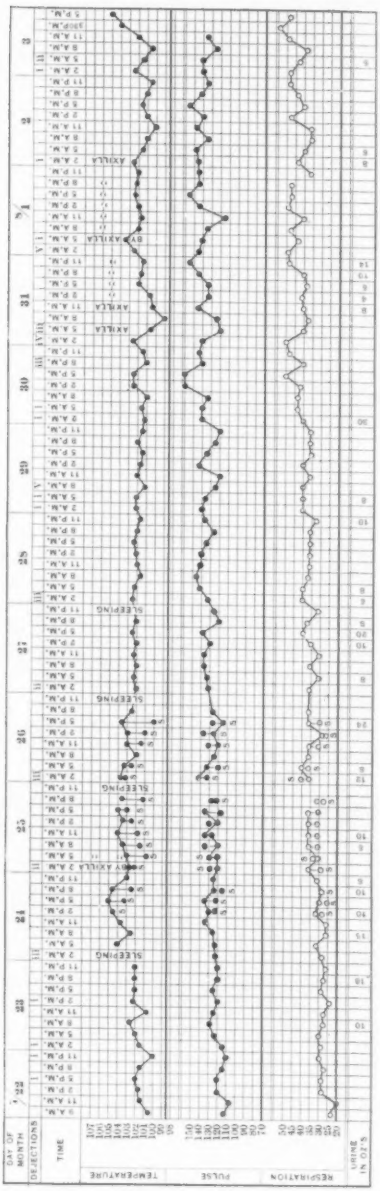

FIG. 1.—Temperature chart.

the conjunctival sac, which was examined for gonococci and other bacteria, with negative result.

When seen in consultation at the request of Dr. Frescoln, and later with Dr. William E. Hughes, the patient was decidedly toxic, though fully conscious, and in evident pain, which she indicated as most intense in the left side low down in the anterior axillary line. She related that three days previously she had a chill, and since then the pain in this location and sometimes throughout the chest had been constant and very severe. The right eye, the orbital tissues, and the eyelid on July 25 all appeared boggy, the temporal tissues were discolored and edematous, and the surrounding scalp suggestive of underyling infection.

The patient was of small frame, normal in contour. The skin was sallow, but not distinctly jaundiced. The whole of the right half of the scalp was involved in a cellulitis, which caused a dark bluish color of the tissues, through which numerous pustular openings discharged each about a drop of greenish-yellow pus. There were no other suppurative foci on the surface of the body. The cardiac rate was then 120 to 140, the respirations averaged 30 to 35, and there was much distress on breathing and coughing, mainly, as before, on the left side. There was also a small area in the left posterior chest near the angle of the scapula that, even to the lightest plapation, was exquisitely tender. Over the entire left lung a harsh friction was audible, heard loudest and evidently produced over the left scapular region. No rales were audible as yet over the left lung. Over the right lung the breath sounds were comparatively free, though over the right base posteriorly were heard a few tiny crackling rales.

On July 26 the patient experienced much distress from pain and labored breathing. On this day there also appeared a profuse urticarial eruption, whether as the result of small doses of quinine (1 grain three times daily) or of the toxemia did not appear clear at first, though on the withdrawal of the quinine the urticarial wheals gradually changed into hemorrhagic areas, some petechial others extensive in size. A few of the smaller petechiæ presented a tiny pustule in the centre. The patient also began to expectorate bloody mucopus and gave signs of widespread consolidation behind and below the left scapula. Loud, metallic, crackling rales became audible over the left axilla, and soon extended over the entire anterior lower lobe. The right eye and the surrounding tissues were more and more involved in a virulent suppurative infiammation, and pus extruded from dozens of small openings over the entire cranial surface.

On August 1 the pain and dyspnea were extreme; the patient was jaundiced and deeply toxic; the tongue dry and parched, and the abdomen greatly distended. Air hunger was intense. At this time there occurred a syncopal attack that caused the patient to appear

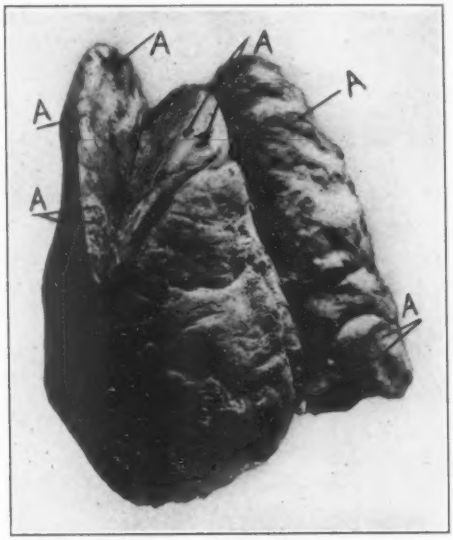

FIG. 2.—Lungs containing numerous abscesses (*A*).

FIG. 3.—Heart, showing metastatic abscesses (*A*) near apex

FIG. 4.—Heart, showing portion of large pus collection (*A*) in left ventricle wall.

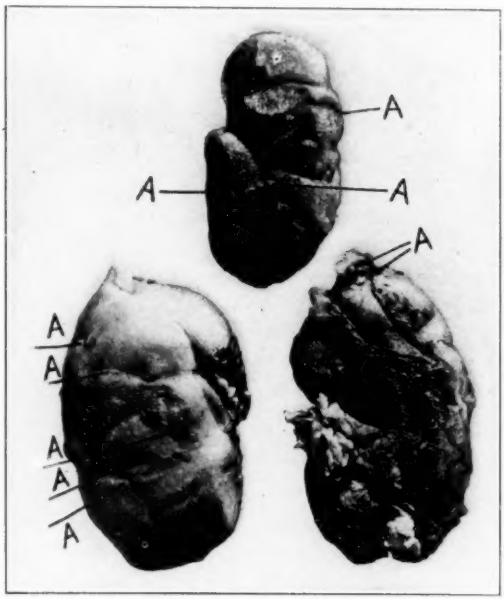

FIG. 5.—Kidneys, the seat of many small abscesses (*A*).

moribund. Free incisions had been made in the scalp early in the morning of this day by Dr. M. G. Warmuth, and a large quantity of thick greenish pus was evacuated through the incisions and through the myriad carbuncular openings. From the pus staphyloccocci only were obtained. An autogenous vaccine had been prepared from the micrococci obtained in the scalp pus earlier in the history of the case, and was used on this day, but without evident benefit. A pure culture of pneumococci was eventually obtained from the blood.

On August 3 the patient became even more deeply jaundiced, expectorated pure blood, and was evidently dying. Large metallic rales were heard over the entire left anterior chest (the patient was at this time too ill to examine needlessly). The next day she seemed for the moment stronger and more comfortable than at any time. The mind was again clear, the patient asked for food, said she was hungry, and took considerable interest in her surroundings. She again became toxic in appearance, however, and at 7 P.M. suddenly collapsed and died.

Autopsy Record. On August 5 section was made of the body, which had already been embalmed. The tissues were deeply bile-stained and of a deep saffron color, except the scalp, which was of a dark purple hue. Everywhere over the body were the petechial and ecchymotic areas noted during life. On opening the thorax the lungs were seen to be adherent at all points of contact with the pericardium. About one pint of seropurulent fluid was removed from each pleural cavity. Everywhere were also extensive adhesions binding the lungs to the thoracic wall. Both lungs were riddled with abscesses (see Fig. 2), the pus from which contained in every microscopic field a few pneumodiplococci. The heart was dilated, and the muscle, though hypertrophic, was flabby and weak. In the myocardial wall were multiple metastatic abscesses, several on the surface of the heart near the apex (see Fig. 3), and one large pus collection just below the anterior coronary opening in the left ventricular wall (see Fig. 4). Smears from the pus in the myocardial abscesses were examined, and in all were found great numbers of pneumodiplococci, as contrasted with the very few detected in the pus obtained from the pulmonary foci.

The kidneys also presented many small abscesses (see Fig. 5), both upon the surface and within the parenchyma. Two infarcts were found in each kidney. The spleen contained one small abscess beneath the capsule. The liver showed marked congestion and some fatty degeneration, but no localized pus foci. There was about one pint of clear serum in the abdominal cavity. The stomach, intestines, pancreas, and uterus and appendages all appeared normal.

AORTIC REGURGITATION.[1]

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It is not the object of this paper to present a complete study of the subject of aortic regurgitation, but simply to discuss some of the mechanical factors that come into play as a result of the lesion and contribute both to the physical signs and to the secondary changes in the heart itself. Occasionally it happens that valvular lesions are regarded too much from the mechanical standpoint, to the exclusion of other important conditions, but, on the other hand, they must not be overlooked, because the more perfectly we understand the different influences at work in each case the more probable is it that we shall be able to make life comfortable for the patient.

Factors Influencing the Momentum of the Regurgitant Stream. During diastole a stream of blood flows backward from the aorta into the ventricle with a momentum resulting from a number of factors, none of which are constant. (1) Gravity which must depend upon the position of the patient. (2) The recoil of the aorta, the walls of which have been stretched during systole, will naturally vary with the volume and force with which the ventricular contents have been propelled into the aorta, the condition of the aortic wall, and the degree of contraction in the peripheral vessels. (3) The ventricular suction at the commencement of diastole, which is only of momentary duration, and corresponds to the elastic recoil or relaxation of the myocardium rather than to active diastole, for at no time is the ventricular cavity a vacuum; nevertheless, this short negative pressure gives an initial impulse both to the auricular direct and aortic regurgitant streams. It is evident that in feeble cardiac contraction there will be little, if any, elastic recoil of the myocardium, and consequently this negative pressure may be entirely absent. (4) The effects of this stream will also be influenced by the area of the regurgitating column of blood, that is, by the size of the aperture of incompetence. All of these factors contribute toward the momentum of the regurgitating blood stream, and all of them are liable to vary from time to time in the same patient.

The Distribution of the Diastolic Murmur and Conditions Influencing It. This depends upon the direction of the regurgitant stream, which is modified by the nature of the valvular lesion and also by the force of the current; but both of these have to be considered in relation to the anatomical formation of different parts of the ven-

[1] Read before the San Francisco County Medical Society, March 14, 1911.

tricular walls, as well as in connection with the fact that the blending of the aortic regurgitant stream with that entering through the auriculoventricular orifice is liable to produce vibrations within the ventricle that are communicated to the cardiac wall, and thence to the chest wall and ear of the auscultator.

The diastolic murmur which accompanies this condition is recognized by most clinicians to be the most erratic of all cardiac murmurs in its area of distribution. The maximum intensity is most frequently not in the so-called aortic area, but over the *left* half of the sternum at the level of the third interspace or upper border of the fourth costal cartilage, or it may be over the right side of the sternum at the level of the third interspace, or at the apex and only at the apex. Furthermore, the distribution is not always the same from day to day in the same patient.

For more than twenty years, in consequence of experimental data, and also because of observation made in the postmortem room, an attempt has been made to infer from the direction in which the murmur is propagated which valve segment is affected, for it is very evident that the direction of the regurgitant stream must be influenced by its own force and by the position and character of the valvular aperture. Injuries of the left cusp tend to deflect the stream toward the septum, while those of the posterior cusp incline it in the direction of the apex, and those of the right cusp allow it to impinge upon the aortic segment of the mitral valve. This applies to perforations of the segments artificially produced, but pathologically the orifices permitting incompetence are generally between the margins of the segments, of irregular outline, with some parts of the valve more distorted than others, and in this way they are calculated to deflect the stream in an irregular manner, similar to that in which the direction and arrangement of a stream of water is changed when it passes through the battered orifice of a metal nozzle.

In cases of combined stenosis and incompetence the regurgitant stream must, in some instances, flow over vegetations projecting from the anterior portions of the cardiac surfaces of the aortic valves or from the wall of the aortic vestibule, and in this way modify the character of the murmur.

Again, variations in the area of distribution of the murmur in the same patient from day to day, apart from those cases of acute endocarditis, where the inflammatory process is continually changing, are probably due to variations in aortic pressure. If the left ventricle of a bullock's heart be opened without doing injury to the aortic valves, one of the segments perforated and water forced through it from the aorta by means of a pressure bottle, the direction of the stream will be modified by the pressure, because the water tends to flow through the orifice at right angles to the plane of the valve at that particular point. But as the surface of the valve is a

curvature, and as the valve contains elastic tissue, the relation of the aperture to other parts of the heart will vary with the degree to which the segment is stretched. This will be even more conspicuous in disease, for the margins of the valves are never identically injured in corresponding places, and according as the lunules are more or less distended, so will the coaptation of the three segments be modified, the shape and attitude of the incompetent orifice changed, and the direction of the blood stream correspondingly altered. Furthermore, the greater the force of the regurgitant stream, the longer does it persist in its original direction and the greater is its momentum within the ventricle, so that more powerful intraventricular vibrations are produced and conveyed to the cardiac wall.

But there are certain anatomical features of the cardiac walls that assist in conveying intracardiac vibrations to the chest wall. "The muscular portion of the wall of the left ventricle attains its minimum thickness at the apex, but the thinnest portion of the boundary is at the upper part of the septum, which consists entirely of fibrous tissue."[2] The septum extends from the right of the apex to the interval between the pulmonary and aortic orifices, that is, to a point behind the left half of the sternum at the level of the third costal cartilage.

It is peculiarly signficant to notice how frequently murmurs of aortic incompetence have their area of maximum intensity at some point along this line, namely, an oblique line extending from the middle of the sternum at the level of the third costal cartilage to a point inside the apex, and it is still more suggestive when taken in conjunction with the fact that on the left side of the membranous portion of the septum is the vestibule of the aorta, because observation has shown that injury to the left aortic cusp tends to direct the regurgitant stream against this portion of the septum. It is, therefore, highly probable that in many cases of aortic incompetence the interventricular septum plays a prominent part in conveying intraventricular vibrations to different points on the chest wall and to the ear of the auscultator.

It is probable that there is still another factor in the production of the aortic murmur which will aid in explaining the vagaries of its distribution and quality. This sound is generally described as if it were produced at the aortic orifice alone and transmitted by the regurgitant stream impinging upon some point in the ventricular wall, but this by no means describes the true condition, because it depicts the ventricular cavity as an empty space into which the blood is pouring. The fact is that there never is a vacuum within the ventricle, but, on account of their elastic and contractile character, the walls are always in close contact with one another or with

[2] Cunningham's Anatomy, p. 791.

the blood contents; in other words, while the ventricular cavity varies in size with the degree of systole and diastole, nevertheless it is always full, even if the contents amount only to one or two drams of residual blood. The regurgitant stream, therefore, pours back into a cavity that is already full and is undergoing further diastole by the blood entering through the mitral orifice, and these two streams meet at some point which will vary with the angle of entrance of that coming from the aorta, their intersection resulting in the production of numerous eddies which may be audible, but which are at least capable of causing vibration in whatever tissues are nearest to the storm centre of the eddy, so to speak. It may be in the mitral valves, or the chordæ tendineæ, or the papillary muscles, and consequently, the line of transmission varies with the particular group of muscular fibers that are connected with the tissues thus agitated.

We are apt to forget or doubt that vibrations produced inside the heart can throw the cardiac walls into vibration, but we must remember that the interventricular septum, the papillary muscles, and the chordæ tendineæ are not outgrowths of some fibrous substance from the inner surface of the heart, but are rearrangements of the myocardial fibers without any interruption in their continuity. Consequently, vibrations produced in these intraventricular projections may be carried along the fibers to their place in the cardiac wall and through the thoracic parietes to the ear of the auscultator.

These intracardiac fibers are represented in different parts of the ventricular walls; some of the parietal fibers from the front and left side enter the base of the posterior papillary muscles, while those from the back and right side terminate in the anterior papillary muscle. "The muscular fasciculi which enter the papillary muscle are continued, by means of the chordæ tendineæ, to the flaps of the mitral valve and so to the fibrous ring around the mitral orifice."[3] It is quite possible that this identity of intraventricular with parietal fibers is largely responsible for the variations in areas of maximum intensity of cardiac thrills and murmurs.

Among other matters of interest in the study of cases of aortic regurgitation are the changes that take place in the left ventricle and auricle. These are frequently discussed as if the enlargement of the ventricle were due to pressure from the volume and force of the aortic regurgitant stream, and the auricular increase were the result of a compensatory effort consequent upon failure of the left ventricle. But for the following reasons it is probable that the changes in the left auricle and ventricle take place simultaneously and that the left auricle is responsible to a very great extent for the dilatation of the left ventricle.

The increased capacity of the left ventricle is the result of a

[3] Cunningham's Anatomy

forcible dilatation, owing to the regurgitant stream entering under pressure at a time when the ventricular walls are relaxed and the blood is simultaneously pouring forward through the auriculoventricular orifice, so that when the auricular systole is due, it finds that it has to discharge its contents into a ventricle which is already better filled than it should be at this period of the cardiac cycle. Consequently, the ventricle must dilate that it may accommodate the additional quantity of blood, or the auricle itself must yield under the strain. Fortunately, the reserve capacity and power of the left ventricle is considerable, so that in very many cases its elasticity permits an increased capacity without the infliction of any injury to the muscle fibers, and the reserve force is sufficiently great to discharge the increased volume of blood into the aorta with each systole, and thereby maintain compensation. In accordance with physiological laws, the cardiac muscle should hypertrophy in response to this increased amount of work, but this process, which is a gradual one compared to that of dilatation, will take place only if the coronary circulation is adequate to supply the demands for increased nutrition, and if the patient's habits are so regulated that he lives well within the working capacity of his heart and allows time for additional muscular growth before attempting any exertion. In cases of the cardiac variety, occurring in young people, it not infrequently happens that perfect compensatory hypertrophy takes place, the increased capacity being sufficiently great to accommodate the additional quantity of blood, and the hypertrophy strong enough to discharge it into the aorta. Such compensation, however, demands (1) that the coronary arteries shall be healthy, hence it is nearly always impossible in the arteriosclerotic variety; (2) that the amount of regurgitation shall be small, because a large amount of regurgitation must quickly lower the aortic pressure and thus interfere with the proper filling of the coronary vessels; (3) that the heart shall not be subjected to any strain while the compensatory hypertrophy is developing. It must not be forgotten that the left auricle participates in producing and maintaining compensation even at this time.

The changes in the left auricle take place simultaneously with those in the ventricle, and are not secondary to ventricular failure. There is too much tendency to attribute the dilatation of the left ventricle to the regurgitating stream alone, but the fact remains that the auricular contraction which completes the ventricular diastole must contribute a very large quota of the distending power; because, no matter how full the left ventricle is of regurgitated blood, the auricle attempts to force its contents forward, and thus, through the auriculoventricular orifice, exercises a pressure which, according to Pascal's hydrostatic law, must be equal in all directions and, therefore, prove to be a powerful factor in stretching the ventricular walls. The left auricle, therefore, from the very first, has

a tendency to hypertrophy in accordance with the physiological law that muscles hypertrophy under increased work, but, of course, the degree of hypertrophy will vary with the amount of work imposed and the capacity for increased nutrition.

It appears to me, from such considerations, that it is a mistake to regard the auricular changes as a result of failure of ventricular compensation, the auricle and the ventricle must suffer together, and when the latter begins to fail from lack of adequate coronary circulation, so will the former. If we accept the idea, so frequently expressed, that auricular hypertrophy does not begin until failing compensation has permitted muscular mitral incompetence, then we must ignore the fact that in cases of aortic regurgitation, the auricle is working against increased resistance, and we must believe the improbability that the same coronary circulation which is inadequate to maintain an established ventricular hypertrophy, is quite capable of producing an auricular hypertrophy. Unfortunately, morbid anatomical statistics are not of much value in enabling us to arrive at a conclusion upon this subject, for while they show that in the majority of instances both auricle and ventricle have undergone changes, on the other hand, those cases have generally reached the stage of muscular failure before death took place, and consequently do not indicate when the process began. Clinical evidence is not wanting to demonstrate that in aortic disease there is an increased intraventricular pressure that extends backward beyond the mitral valve to the auricle and even into the pulmonary system. Hemoptysis, in cardiac valvular disease, is general accepted as a symptom of high pulmonary pressure. Some years ago, at Guy's Hospital, London, statistics were collected from all cases of hemoptysis occurring in valvular disease, with the object of ascertaining the valve lesion in which pulmonary hemorrhage was most common. It was found that 59 per cent. of the cases were, as might have been expected, examples of mitral stenosis, a smaller number presented single or double lesions of the aortic valves, while uncomplicated mitral incompetence furnished fewer examples of hemoptysis than any other valve lesion.

Many years ago Balfour called attention to the influence that the regurgitant stream, operating under Pascal's law, would have in producing ventricular dilatation, but he omitted to mention the much greater results that must be obtained from the left auricle working on the same principle. When we reflect that the capacity of the normal auricle is almost as great as that of the ventricle, and that Pascal's law, which maintains that pressure applied anywhere to a body of confined liquid is transmitted by the liquid so as to act with undiminished force on every square centimeter of the containing vessel, is the principle upon which such powerful apparatus as the hydraulic press and hydraulic elevator are constructed, we can realize what an enormous pressure the auricle exerts upon

the inner walls of the ventricle when it contracts upon that cavity already full of blood.

Arguing from such premises, it would seem reasonable to conclude that compensation for any degree of aortic incompetence from its very commencement depends upon the capacity of the left auricle and ventricle to undergo hypertrophy. But compensation may never take place either because the amount of regurgitation is beyond the combined powers of auricle and ventricle from the very commencement, or the patient is not kept at rest for a sufficient length of time to permit the growth of the necessary muscular tissues, or the condition of the myocardium and coronary vessels may be such as to make hypertrophy impossible. This is especially the case in the arterial variety of aortic incompetence, as this pathological lesion is very liable to be associated with atheroma of the coronary arteries or some other degenerative changes.

It must be borne in mind that in almost every instance, even when the most satisfactory compensation exists, it is only a matter of time until failure will occur, and one cannot help being impressed with the rapidity with which failure progresses when the downward process has once commenced; yet the reason is not far to seek. The continual increase of muscular tissue ultimately puts the myocardium beyond the nutritive power of the coronary vessels, especially in the arterial variety of incompetence. Even in the majority of endocarditic cases the coronary vessels have been taxed to their fullest capacity, and, as the degenerative changes consequent upon the increasing years of the patient are superadded to the original lesion, it is natural that failure should take place rapidly.

As the great majority of cases of aortic incompetence are combined with aortic stenosis, we can readily understand that the dilatation will be still greater; in fact, any disease of the aortic orifice that tends to increase the amount of residual blood in the left ventricle to such an extent as to increase its capacity and offer abnormal resistance to the influx of blood from the auricle must, under Pascal's law, increase to a very great extent the strain upon the ventricular wall during auricular systole. This strain may be within the capacity of the elasticity of the muscular fibers, and under such conditions no harm may result, but if it exceeds this point the lesion must terminate sooner or later in failure of compensation.

Stewart[4] produced aortic insufficiency in dogs by means of MacCallum's valvulotome, and after the operation the animals were kept in a separate room with a yard attached and allowed to run about it at will. The hearts were examined at periods, varying from four days to three months. He obtained a standard by examining twenty dogs and determining the proportion of the total heart weight in each to its body weight, and then the proportional

[4] Jour. Exper. Med., February, 1911.

weight of each left ventricle, right ventricle, septum, and the combined auricles to the body weight, and found that after operation, on making an average of the weights, the heart was approximately one-third larger than normal. The average increase showed 40 per cent. for the total heart, 59.3 per cent. for the left ventricle, 33.7 per cent. for the septum, 10.7 per cent. for the right ventricle, and 50 per cent. for the combined auricles.

Dr. Stewart believes that hypertrophy of the heart is due to increased work; that in the left ventricle the stimulus resulting in increased force of contraction lies in the greater tension applied to the ventricular wall during diastole, the hypertrophy of the septum is simply a hypertrophy of the fibers of the left ventricle that pass through the septum, and the hypertrophy of the right ventricle is confined to the muscular fibers that are common to both ventricles.

It will be noticed that in all cases the auricles were found to be hypertrophied as well as the ventricles, even in the earliest cases, and it is this simultaneous change in auricle and ventricle that has been contended for in an early part of this paper. He does not attribute this auricular hypertrophy to increased resistance to auricular systole, because he did not find "evidence of increased distention such as could be caused by an increased auricular pressure," but he noticed that when the left ventricle was incited to increased contraction there was a sympathetic increase in the force of the auricular contractions. No explanation of this sympathetic action can be given at the present time, but there is strong presumptive evidence of the "existence of an intracardiac reflex which maintains a coördination in the force of the systolic contraction between the chambers of the heart." The observations by Stewart do not in any way invalidate the contention that auricular contraction plays a prominent part in dilating the left ventricle because it is not necessary that an increased amount of blood should be propelled through the mitral orifice, the dilating power lying in the additional amount of blood in the left ventricle, as a result of aortic regurgitation, while the force of the auricular systole remains constant or is increased, as stated by Stewart.

More experiments showed another matter of special interest in regard to treatment, namely, "the remarkable rapidity with which the heart hypertrophies after the production of aortic insufficiency. This hypertrophy is well established after one week, and at the end of five days there is sufficient evidence to show that even the enlargement is in progress." We must remember that Stewart was working with normal heart muscles, and that clinically, where one is so frequently dealing with a co-existence of aortic incompetence and myocarditis, the extent of injury to the left ventricle must vary, but this does not in the least invalidate his conclusions.

Such considerations should not be regarded simply as medical

sophistries of no practical importance; on the contrary, they explain many clinical points and afford the indications for treatment. A thorough appreciation of the manner in which compensation is established and maintained, together with a recognition of the difficulty of restoring compensation when it has been lost, can only be obtained from a perfect knowledge of the cardiac mechanism and the manner in which it is liable to suffer under various abnormal conditions.

It is a fact that in many instances aortic lesions are regarded too lightly at their inception, and a patient allowed to resume active duties before there has been time for sufficient compensatory hypertrophy to develop, with the result that the mitral orifice becomes incompetent, and this is much harder to overcome when associated with an aortic lesion than when it occurs alone. Clinicians will generally admit this to be the case, and it is not difficult to find the explanation. Cases of muscular mitral incompetence can be relieved only by resting the heart and improving its nutrition, and success in the latter direction depends upon the possibility of restoring and maintaining an adequate circulation through the myocardium itself. To attain this end a rise in aortic pressure must be obtained, because this is one of the chief factors in determining the flow of blood through the coronary arteries; but the constricted aortic orifice, by diminishing the volume of blood entering the aorta or the incompetent valves which allow the blood to escape, present obstacles to the production and maintenance of normal aortic blood pressure which do not exist in the uncomplicated mitral lesion.

RECENT ADVANCES IN ANATOMY AND PATHOLOGY OF THE HEART FROM A CLINICAL POINT OF VIEW.[1]

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In a period of transition, such as that which at present involves our knowledge about heart disease, it is difficult to appraise properly what is and what is not important. To sum up the change in viewpoint which the subject is undergoing, it may be said that while up to five or six years ago we concerned ourselves with valvular lesions, and devoted all our energies to diagnosticating them from the point of view of sound and murmurs, and to a less extent from that of dilatation, as evidenced by percussion, palpation, and transillumination, now we have come to regard the heart as a whole, and to

[1]Read before the New York Academy of Medicine, April 20, 1911.

lay more stress on its working muscular portions and less on its automatically acting valves. It is not meant that valvular defects, either acute or chronic, have assumed a subsidiary place in our study, but that muscle function as such has been raised to a position of such importance that phenomena, which formerly were unrecognized clinically, are now capable of furnishing us with much valuable information both from a diagnostic, prognostic, and also, as many are hoping, from a therapeutic viewpoint. If we dismiss valvular diseases, therefore, from this survey, it is not because we consider them unimportant, but because recent advances have not been in their direction.

About thirty years ago Englemann and Gaskell, by extensive experiment, first placed our views about the functions of the heart muscle on a more exact basis. As a result of their work we have now come to speak of the heart muscle as possessing the functions of irritability, contractility, rhythmicity, and conductivity (in Engleman's phraseology, the bathmotropic, inotropic, chronotropic, and dromotropic functions of the heart muscle). We do best when we investigate heart muscle and heart disease under these separate heads, since frequently one patient suffers from a defect of only one of these functions, while another suffers from a combination of two or more, either as the ultimate result of a valvular lesion or, what is coming to be recognized as almost as common, a functional disturbance without the existence of a valvular defect. From a clinical point of view much has been added to our knowledge of rhythmicity and conductivity, but scarcely anything to that of irritability or contractility. As I shall point out, even that function of which we know most, namely, conductivity, leaves many points quite unexplained.

When we investigate the anatomical facts which underlie these functions of heart muscle, we are obliged to subdivide them into those which are muscular and those which are nervous, and to assign to each its proper domain.

The teaching that nerve fibrils surround and themselves interlace about the muscle fibers of the main body of the ventricular musculature is already old and accepted. Much has been added to our knowledge of the location of ganglia within the heart both of man and the lower animals. More recently, Tawara,[2] Wilson,[3] Engel,[4] and others have demonstrated the presence of nerve fibrils in the same sense about the auriculoventricular bundle, described by Kent,[5] His,[6] Braeunig,[7] Retzer,[8] Humblet,[9] Tawara,[10] and in

[2] Das Reitzleitungs system des Säugetierherzens, G. Fischer, Jena, 1906.
[3] Proc. Roy. Soc., 1909, Series B, vol. lxxxi, pp. 151 to 164.
[4] Ziegler's Beiträge, 1910, Band xlviii, 499 to 526.
[5] Jour. of Physiol., 1893, xiv, 233 to 254.
[6] Arbeit. aus der med. Klinik zu Leipzig, Leipzig, 1893, 14 to 50.
[7] Arch. f Anat. u. Physiol., Anat. Abt., 1904.
[8] Ibid.
[9] Arch. Intern. de Physiol., 1904, i, 278 to 286.
[10] Loc. cit.

some species have even shown that ganglion cells can be found far down in the ventricle in close union with the ventricular branches. These anatomical facts are known, but as yet nothing has been added to our knowledge of their function, and, more especially, no clinical abnormality has been correlated with a defect or lesion involving them. Furthermore, although a considerable literature has been accumulated in relation to the extrinsic nerves and central ganglia, both anatomical and physiological, it must be confessed that, in spite of the many facts collected in regard to the action of the vagi, the accelerators, and the depressor nerves, clinical knowledge of them is very deficient, and in many respects absent. Finally, it may be pointed out that there exists practically no investigation which relates the paths and distribution of the extrinsic with the system of intrinsic cardiac nerves.

The most that can be said is that certain manipulations of the extrinsic nerves produce certain effects and that the calling forth of these effects are very limited in number and are not constant phenomena. Here then is a large though difficult field for future investigation, and it would seem that, until much more knowledge along these lines is at hand, a myogenic and a neurogenic doctrine may be useful as points of view from which to investigate, but these doctrines should certainly not furnish a basis for the erection of hostile camps, from both of which polemics constantly keep pouring forth.

The study of the muscular architecture of the heart has brought us a large body of facts which have proved clinically extremely useful, even though this study has been concerned only with the functions of conduction and rhythm. Great advance was made after Gaskell and Englemann gave utterance to the doctrine that the propagation of an impulse once formed was conducted to other and appropriate locations in the heart by means of the heart muscle, and that in the muscle as such resided this function of conduction. Unfortunately no muscular connection between auricles and ventricles was known in the eighties, and it was not until 1893 that anatomical confirmation was given this theory by Kent[11] and His, Jr.,[12] who found what is now recognized as the auriculoventricular bundle. Braeunig,[13] Retzer,[14] and Humblet[15] confirmed the existence of this structure, but it remained for Aschoff and Tawara[16] to find its beginning in the lower interauricular septum and its ending at the venous base of the heart, in the papillary muscles. At the beginning of this conduction system and where the auricles join it, Tawara described a structure which is now called by his name, the node of Tawara, quite different in its anatomy from the rest of the heart muscle.

[11] Loc. cit. [12] Loc. cit. [13] Loc. cit.
[14] Loc. cit. [15] Loc. cit. [16] Loc. cit.

A point which should be clearly made is that no part of this A-V system should be called embryonic or an embryonic remains. Whoever has examined embryo hearts will know that it has no similarity with embryonal cardiac muscle. And Keith[17] has said: "If by embryonic is meant that they resemble the cardiac fibers of the heart of the embryo, then nothing could be further from the truth; if by embryonic is meant the fact that only the superficial stratum of the fibers is striated, the interior being undifferentiated cell substance, then in this feature they are embryonic. They are cardiac fibers which have specialized in a peculiar direction; their fibrillar structure is especially distinct."

To return, however, to the node of Tawara. Much has been written about its function, both as a pacemaker for the heart in abnormal conditions, a function once ascribed to it by Mackenzie, but now entirely abandoned by him, and as a site for the formation of so called atrioventricular extrasystoles. Actually there is known to us only one series of experiments which has been able to ascribe a definite function to this structure, and this is contained in a paper by H. E. Hering,[18] in which he maintains that the node of Tawara delays conduction. He ascertained this fact by stimulating below the level of the node and calculating the conduction time from the instant of stimulation until there occurred contractions of the auricle on the one hand and the ventricle on the other, and from these making the necessary deductions. Further than this nothing is known about the node. Aside from the node and bundle, the demonstration of nerve trunks, nerve fibers, and nerve ganglia in the conduction system, and a demonstration of the constant union of the A-V node with the auricles—a point that was necessary to complete the knowledge of the anatomical path and to show that normal automatism was a function which need not be ascribed to the auricle any more than to the ventricle—complete our anatomical knowledge about the auriculoventricular conduction system.

Knowledge about rhythmicity was augmented by the description of a node similar in structure to Tawara's in the wall of the right auricle, by Keith and Flack.[19] It begins at the junction of the superior vena cava and the upper border of the right auricular appendix and extends from there downward a varying distance in the direction of the sulcus terminalis. Structures similar to this are found at other sites, and may ultimately be shown to have functions not now ascribed to them, but we will at this time neglect them. The sino-auricular node has communications with auricular musculature in every direction. Its site and microscopic anatomy have

[17] Lancet, 1906, ii, 359 to 364.
[18] Pflüger's Arch., 1910, cxxxi, 572 to 581.
[19] Jour. Anat. and Physiol., 1907, xli, 172 to 189.

been confirmed by Koch[20] and other observers. That rhythmicity—stimulus production—has its seat in this node and that it acts under normal conditions as the pacemaker of the heart, was a function originally claimed for it by Keith. That this function resided in this region had been presumed by McWilliam,[21] Adam,[22] Langendorff and Lehmann,[23] Erlanger,[24] and Hering.[25] Since then, except only the negative experiments of Jaeger[26] and Magnus-Alsleben,[27] investigations by Lewis,[28] Lewis and Oppenheimer,[29] Wybauw,[30] Cohn and Kessel,[31] have tended to support and confirm this view.

I have said that the sino-auricular node communicates at its entire circumference with the auricular muscle. Thorel[32] imagined, however, that a communication between it and the A-V node was necessary for physiological reasons. The assumption was not, however, required by what is known of muscular conduction, and was not borne out by many other observers who failed to substantiate his anatomical findings. From the point of view of anatomy, therefore, counting more especially from the time of Braeunig and Retzer, the last seven years have put us in possession of the sino-auricular node, described by Keith and Flack, in which most probably resides the pacemaking function of the heart; and of the auriculoventricular system, through which stimuli pass from the auricles to the ventricles, so maintaining correlated contraction between these two pairs of cavities.

When we turn to that portion of the pathological anatomy of the heart which deals with the four divisions of its function above named, we find again, and naturally, that investigation has been confined only to the functions of rhythmicity and conductivity. It may be that the other functions have no anatomical substratum, and it may also be that all the functional deficiencies in these two, that is, rhythmicity and conductivity, cannot be explained anatomically, but the fact remains that anatomical explanations are at hand only for these two.

Sixty per cent. of all cases of irregularity of the heart fall under the heading of the so-called pulsus irregularis perpetuus, known also as the completely irregular pulse, nodal rhythm, and indeed by a variety of other names.

[20] Deutsch. med. Woch., 1909, No. 10, pp. 429 to 432.
[21] Jour. of Physiol., 1888, ix, 167.
[22] Pflüger's Arch., 1906, Band cxi, 607 to 619.
[23] Ibid., Band cxii, 352 to 360.
[24] Amer. Jour. of Physiol., 1907, xix, 125 to 174.
[25] Pflüger's Arch., 1907, cxvi, 143 to 158; Münch. med. Woch., 1909, lvi, 845.
[26] Deutsch. Arch. f. klin. Med., 1910, Band c, 1 to 11.
[27] Arch. f. exp. Path. u. Pharmak., 1911, lxiv, 228 to 243.
[28] Heart, 1910, ii, 23 to 47.
[29] Ibid., 147 to 169.
[30] Arch. de Physiol., x, i. Quoted from Münch. med. Woch., 1911, No. 4, p. 215.
[31] Arch. Intern. Med., 1911, vii, 226 to 230.
[32] Münch. med Woch., 1909, No. 42, p. 2159.

The history of its explanation is an interesting example of the history of anatomical and physiological advance. When Mackenzie[33] first described the condition, he believed it to be due to auricular dilatation and paralysis. At that time the anatomy of the A-V system was practically unknown. But paralysis meant atrophy, and Mackenzie soon saw that cases with a pulsus irregularis perpetuus might actually show hypertrophy of the right auricle. Then it happened that the A-V node, supposed to be embryonal in structure and therefore of pacemaking fiber, was credited with the function of stimulus production. Lying between auricles and ventricles, and almost equidistant between them, impulses starting here and going in both directions would arrive at and set in motion both pairs of cavities at the same time. The explanation was simple; it accounted for the auricular hypertrophy, for the auricle kept beating; it accounted for the absence of the A-wave in the jugular pulse, since auricles and ventricles would be beating synchronously; it even accounted for the increased auricular rate often found. At the same time, to lend weight to the theory, Keith found a variety of lesions in and about the A-V node and bundle; these formed the factors which were alleged to irritate the A-V node to increase its activity.

The explanation neglected, however, the doctrine that automatically beating heart portions beat regularly and not irregularly, and herein lay the weakness of the explanation, a weakness that had been pointed out as an *a priori* objection. The explanation was, however, held until the fall of 1909, when Lewis,[34] and Rothberger and Winterberg[35] were able to demonstrate conclusively that the irregularity was due to auricular fibrillation, a theory which explains auricular hypertrophy, an absent A-wave from the jugular pulse, and by comparing the experimental with the clinical tracings, the perpetual irregularity as well.

Now the anatomical interest shifted from the A-V system to a study of the right auricle. Schönberg,[36] Hedinger,[37] Koch,[38] have reported histological studies in this region, while many others are still in progress. The first studies of Schönberg and Hedinger may be briefly dismissed; they concerned themselves with lymphatic infiltration in a strand of auricular muscle which ran from behind and below, upward and forward on the superior vena cava. Wenckebach has supposed that if stimuli were produced at the entrance of the great vein to the auricle, over this pathway the stimuli must be conducted to the auricle. This notion is, of course, no longer held, and therefore lesions in this area no longer deserve the

[33] Brit. Med. Jour., 1904, i, 529.
[34] Heart, 1910, i, 306 to 372.
[35] Pflüger's Arch., 1910, Band cxxxi, 387 to 407.
[36] Frankfürter Zeitschr. f. Path., 1908, ii, 153 to 180; ibid., 462 to 485.
[37] Ibid., 1910, v, 296 to 322.
[38] Berl. klin. Woch., 1910, 1108 to 1112.

attention they once received, nor have they the significance once attached to them. In the sino-auricular node, however, Koch and others have found subendocardial fatty infiltration, small hemorrhages, subacute inflammatory changes, injuries to the nerves and ganglia by connective-tissue growth, occasional lesions in the afferent vessels, and more or less diffuse connective-tissue proliferation. These lesions cause destruction of the structures of the sino-auricular node. Such lesions, not by any means uniform, nor all found in any one heart, are designated as lesions sufficient to injure the pacemaking function of the node and so induce either fibrillation directly, or, in any event, to remove the controlling influence of the sinus, in such a fashion as indirectly to permit fibrillation to ensue. As I shall point out later, in speaking of the lesions of the A-V system, enough cases have not yet been examined nor sufficiently examined to make it advisable to correlate definitely anatomical lesions with functional change; in short, to make the anatomical changes sufficient explanation for the onset of fibrillation. Furthermore, it must be borne in mind that perpetual irregularities are of varying rates, now slow, now fast, and that there are cases in which the rate changes several times during the progress of the case. Therefore, while these anatomical advances and findings are valuable, interesting, and possibly final, enough is not known to consider them conclusive, and harm rather than good may be done by accepting them now.

I turn now to what is known of lesions of the auriculoventricular system and their clinical manifestations. So far isolated lesions involving either the auriculonodal junction or the auriculoventricular node itself are not known. Lesions have been described here, such as subacute, acute, and gummatous inflammations, but these are correlated with no clinical manifestations and require no further notice. When we go on to the main stem, however, a variety of lesions are noted. These may be divided into those which form complete transverse lesions of the bundle, in the same sense that there are complete transverse lesions of the spinal cord, and incomplete transverse lesions. This latter group contains both disseminated lesions and lesions which do not completely divide the bundle.

In the group of complete transverse lesions are enumerated tumors, both benign and malignant, metastases or infiltrations; inflammations, usually syphilitic, among which the calcified gumma plays an important part; and degeneration due to vascular disturbance, either thrombotic or embolic, or endarteritic. These complete lesions, so far as I know, all cause complete auriculoventricular dissociation, and may or may not be associated with the Adams-Stokes syndrome.

In the second group are those cases in which the lesion does not divide the A-V bundle completely. In these there are found the products of chronic inflammation, firm old connective-tissue

infiltration of the main stem, and infiltrations with rather large quantities of fat tissue. A special type consists of the presence in the bundle of large blood sinuses which have materially reduced the diameter of the bundle. It must be confessed that in the group of incomplete transverse lesion, cases are found where the auriculoventricular dissociation is complete, and others where it is partial. Whether the amount of injury alone is responsible for the varying degree of block or whether additional factors related to nerve control, nerve destruction, or nerve tone, are here involved, more expecially in the cases of complete dissociation, cannot now be properly appraised.

A third group[39] of cases must be added in which there are marked lesions of the bundle, but in which, clinically, all types of heartblock are demonstrated, from lengthened A-C intervals to complete dissociation, changing from one form to another in rather a startling fashion. To account for such cases, it has been supposed that the block has been from time to time increased and then diminished by the presence of inflammatory processes which undergo exacerbations and then subside, and which in their organization tend effectually ultimately to destroy the bundle.

In addition to these three groups is a fourth, in which heart block has existed clinically for years, as in Krumbhaar's[40] case, in which a lesion commensurate with the clinical findings cannot be demonstrated. In fact, it can be shown that the hearts in such cases contain lesions less in amount than are observed in hearts known to present no manifestation of disturbed conductivity during life.

Finally, there are a few cases in a fifth group in which, through inflammation or otherwise, one or other of the ventricular branches of the A-V system have been found cut off from the main stem. These cases reported by Eppinger,[41] aside from rather vague but certainly distinct clinical manifestations, have been diagnosticated electrically, and are of great clinical interest.

We have now summed up lesions in the heart involving the sino-auricular node and having their expression possibly in the cases of perpetual irregularity. We have also shown what lesions occur in the auriculoventricular system, and have shown their relation to heart block. We have not considered a number of the other irregularities, also chronotropic functions, expressed in extrasystoles and in praoxysmal tachycardia.

Whether chronic and acute interstitial myocarditis plays a role in the production more especially of ventricular extrasystoles is not known. The assumption is held, nevertheless, and the cases are called cases of cardiosclerosis. It is, however, a fact that there is no definite correlation known as yet between abnormal structure

[39] Quart. Jour. Med., 1910, iii, 126 to 152.
[40] Arch. Int. Med., 1910, v, 583 to 596.
[41] Zeitschr. f. klin. Med., 1910, Band lxxi, 157 to 164.

and abnormal function in any of these cases, nor are the limits of structural change in general convertible into the extent of functional deficiency. An attempt in this direction has been made by Moncke-berg[42] when he considered certain cases of sudden death due to fatty degeneration of the A-V bundle, but his findings have been both confirmed and denied by Engel,[43] and their status is not secure.

Aside from the functions mentioned, little is known. Much is left to be investigated, notably in the domain of irritability and of contractility of heart muscle, expecially in acute infections and in chronic degeneration. The string galvanometer, which produces electrocardiograms, at first seemed destined to help in directing these investigations, and likely much remains for it to do. From the point of view of these functions, anatomy has at this time little in the way of explanation to offer.

In these days, when we are set about by tracings made in a variety of ways, by instruments that detect numerous different physiological activities, and by the effort to understand the meanings of the tracings once obtained, one must insist and insist strongly that all this is but machinery, nothing but a means to an end. It is as aids in understanding the heart in health and disease that this cumbrous apparatus is called into being. The tracings which they yield will be exceedingly barren, unless the effort to interpret them from the standpoint of anatomy and of physiology, both normal and abnormal, is constantly made.

[42] Untersuchungen über das Atrioventrikular bundel im menschlichen Herzen, Fischer, Jena. 1910.

[43] Loc cit.

REVIEWS

JOINT TUBERCULOSIS. By LEONARD W. ELY, M.D., Consulting Orthopedist to the County Hospital, Attending Orthopedist to the Children's Hospital, Denver, Colorado; formerly Surgeon to the Sea Breeze Hospital, and Consulting Orthopedist to the Roosevelt Hospital, New York City. Pp. 243; 72 illustrations and a colored frontispiece. New York: William Wood & Co., 1911.

THIS is a very interesting book. It was begun by the author as a clinical study, but finding this inadequate to explain the phenomena of joint tuberculosis, he turned to the pathology, and, from an examination of 72 specimens from 64 patients, has come to some conclusions which must be regarded as of far-reaching importance if their truth be substantiated by further observation.

He found both osseous and synovial lesions as the primary focus, the latter very rare in children, but much more common in adults. Obliterating endarteritis was observed as a frequent characteristic in these tuberculous lesions.

The localization of tuberculous foci in the epiphyses of children he explains solely by the presence there of red marrow. Where red marrow exists there is a predisposition to the development of tuberculous lesions; and where there is no red marrow the bone is almost immune to infection by tubercle bacilli. Other explanations, he says, such as the lack of terminal anastomoses predisposing to embolism, do not explain. If red marrow can be converted into yellow marrow, tuberculous lesions will heal. He regards lymphocytic aggregations around tubercle bacilli not as the *result*, but as the *cause* of the tuberculous focus; lymphocytes, he contends, as well as connective tissues which contain epithelial, epithelioid, or lymphoid cells, are the natural food of tubercle bacilli; where these elements are not already present, tubercle bacilli do not thrive. He doubts the existence of primary fascial tuberculosis because there exist in fascia no cellular elements suitable for the nourishment of tubercle bacilli.

From these pathological inferences—for at present they can scarcely be said to be more—the author finds a ready explanation of and indication for treatment. *Rest* is the main therapeutic indication, and it succeeds not because of either traction or fixation, which

are mere secondary means of procuring local rest, but simply because it abolishes the function of the joint; and as the function of a joint depends on the existence of red marrow and synovia, the disappearance of these structures, which is encouraged by disuse, promotes cure of the disease; since, where they are not, joint tuberculosis cannot exist. Cure which follows operation is obtained by securing ankylosis (*i. e.*, joint rest); it matters not how little tissue is removed, nor how much tuberculous material is left behind; so long as bony or firm fibrous union is obtained a cure will result, because ankylosis will cause disappearance of red marrow and synovia, without which joint tuberculosis cannot exist. He dilates on the futility of seeking to obtain cure by removal of all the tuberculous tissue; this is absolutely impossible. Resections should be done with the sole idea of securing ankylosis. Cure following excision of the hip, in which ankylosis does not occur, he attributes to the resulting pathological dislocation, which abolishes the joint tissues as such quite as surely as does ankylosis. Curettement and gouging he regards as useless always, and generally as harmful.

From these general principles of surgical treatment, the author proceeds to specific indications. Operations in children are condemned, because they are crippling, and the disease, if taken in time, usually is easily cured without. He seems to be partial to the weight-bearing treatment of hip tuberculosis by means of the short spica of Lorenz, because it promotes ankylosis; and if the disease in any joint is once cured by ankylosis, malposition, if present, can be corrected by osteotomy. As the disease, even when apparently cured by firm ankylosis, is in most cases not really cured, but merely indefinitely quiescent, he condemns, and we believe with entire justice, attempts to secure motion by arthroplasty in tuberculous hips. In adults ankylosis should be secured by operation before secondary infection renders amputation necessary; for without ankylosis or amputation cure need not be expected.

If sinuses are present, with secondary infection, tubercle bacilli can live in the walls of such sinuses; but if an uninfected sinus leads to an uninfected tuberculous joint, its walls will be free of tuberculosis. Hence, before operating on joints with secondarily infected sinuses with the idea of radical cure, it is desirable first to secure closure of the sinuses.

There is an appendix to the book, consisting of case histories which seem to be entirely useless for either pathological or clinical study, owing to the incompleteness with which they are recorded. References to literature throughout the volume should have dates of publication added, as only thus can the reader know whether the authority quoted is still worthy of credence. Clinically, the book is sketchy and incomplete. Pathologically, it is highly suggestive, but not entirely convincing. We shall hope for a second edition supplying these defects. A. P. C. A.

FOODS AND THEIR ADULTERATION. By HARVEY W. WILEY, M.D., Ph.D., Chief Chemist U. S. Department of Agriculture. Second edition; pp. 641; 98 illustrations. Philadelphia: P. Blakiston's Son & Co., 1911.

IN undertaking to review a book such as Dr. Wiley has written, the reviewer must at the outset confess either to a working knowledge of the subject or to absolute ignorance of the whole field. He pleads guilty to the "soft impeachment" of the latter.

To the reviewer, whose task at the present writing is one laid in pleasant ways, the work is the first of its kind which has come to his notice, and his memory fails to recall an instance where an author has so interestingly developed a table of contents which at first blush seemed so dull. To pretend that, at one reading alone, one is in a position to criticise justly a book of such magnitude were presumptuousness indeed, so that here is recorded nothing more than general impressions.

In the main this second edition follows closely the general lines of its predecessor, except that the rules and regulations for the enforcement of the Food and Drugs Act have been omitted.

The author, we fear, presumes too much on the knowledge of the medical man at least, when he offers "such wide distribution" of these rules as a reason for the omission. For the expert, perhaps, but for the medical world at large, who should certainly possess this book, we feel that the reason is not wholly sound. The place left vacant by the deleting of this very important part of the first edition has been divided between a new section on infants' and invalids' foods and one devoted to simple tests for ordinary adulterations.

These two sections have claimed the reviewer's close attention. The former is valuable, but it is questionable whether its insertion in a book of this nature is a particularly happy choice, inasmuch as the work is dedicated to a consideration of foods and their adulterations. We think the section with which Dr. Wiley has seen fit to replace that spoken of above would find a more appropriate environment in works devoted more especially to dietetics. It adds little to the volume unless the possessor of the latter be of the laity, who wishes in one book to have as complete information regarding foods as possible.

The part on detection of food adulterations is written especially for the great mass of people called the general public, but we fear that Dr. Wiley, in his zeal for the cause of the greatest good to the greatest number, has endowed the general public with unusual intelligence when he says of the "simple tests," that "anyone without the training of the professional chemist" may practise them. We very much fear that not every housewife would make much out of the test, for instance, given on page 611.

This book, which must be regarded as an expression of Dr. Wiley's

monumental governmental activities, is a classic. His great work under the Department of Agriculture is so well known that all classes of people regard the name of "Wiley" as one to conjure by. So great has been his work and so vast his field of endeavor, that few realize concretely just what he has done. With becoming modesty, the writer has submerged himself in his book, but they must be blind, indeed, who cannot see that such a work could not have been written without the brilliant researches of Harvey W. Wiley.

It is a valuable volume for all those interested in the science of foods, and, while not indispensable to the practising physician, should not be overlooked by him if he wishes to keep abreast of a question which is claiming more and more attention from the world at large, more familiarly known as the General Public. E. H. G.

THE NERVOUS LIFE. By C. E. PARTRIDGE, Ph.D., Formerly Lecturer in Clark University. Pp. 216. New York: Sturgis & Walton Company, 1911.

THIS is a first-rate work. Within the last few years there have been many popular books on the different "mental worries" and other nervous phenomena, which, according to their authors, seem to be the burden of the human race. The author approaches his work from the standpoint of both disease and health, and argues that the same principles of living are applicable to both. He first takes up the question of the normal life of the individual and the causes which tend to bring on a nervous condition, and then discusses the cure by normal readjustment through normal living. Dr. Partridge has treated the matter in a thoroughly commonsense fashion, and, after all, there is no higher praise than this.

The reviewer, a neurologist, modestly disagrees with the following: "The day has come when we can no longer go to the doctor to be cured of all our ills. Ills have multiplied faster than the doctor's medicines, and personalities have grown so varied and complex that everyone must, to a certain extent, work out his own salvation. It is, indeed, in the most intimate and personal parts of one's life, where neither physician nor other outsider can be competent to advise, that the most pressing of problems are to be found and the best work of self-study can be done." It is true that ills have multiplied faster than doctors' medicines, but then it must be recalled that the up-to-date physician who understands the modern psychological method of treatment of nervous diseases does not give a medicine for every ill. He knows better. He treats the patient. Again, it is all well enough to state that the most pressing

personal problems must be settled by one's self; but suppose the person is not competent to settle this question by himself, what then? Would it not, after all, be best for the patient with mental ills to go to a competent physician who can show him how to solve these problems?

Even such books as this cannot settle all questions for all persons. As a matter of fact, no better argument can be given for the increase of nervousness than the quantities of books which have been published and the many cults which have arisen. Every day one is confronted with some new "pathy" or new method of curing disease. This is partially because many physicians do not understand or do not realize that to treat nervous diseases one should treat the person, and by treating the person one does not mean giving medicines, but handling the patient psychologically; but the principal reason for the growth of osteopaths, Christian scientists, and others is because human nature, at least so far as the neurologist sees it, is frail. (The reviewer, who is a disciple of Bernard Shaw and incidentally of his "Doctor's Dilemma," does not claim this as an original discovery.) If the doctor were to promise that he could cure every and all diseases as definitely as does the Christian scientist and the osteopath, and if he had the ever-present and most splendidly conceived loop-hole that the Christian scientists have—that is, if one does not get better one does not have sufficient faith—then perbaps we would be on a par with them, but Heaven forbid! T. H. W.

Die Behandlung der Frauenkrankheiten. The Treatment of Diseases of Women. By J. Veit, M.D., Professor and Director of the University Clinic for Women at Halle. Pp. 242; 34 illustrations. Berlin: S. Karger, 1911.

This book begins with an observation so sensible that one wonders that it should be mentioned, and yet so essentially practical and useful that it lies at the foundation of all success in treating the diseases of women. Veit urges that in these cases the patient be treated from the objective standpoint only, and that the subjective element in the case be reduced to the lowest possible terms. When one considers how misleading are the symptoms often reported honestly or otherwise by women, and into what serious error they sometimes lead, this caution will be appreciated.

The book begins by treating of disinfection, the use of instruments and minor methods of treatment before proceeding to the operative side. Veit urges that before examinations strict antisepsis should be observed, a caution which is often neglected. He still seems to have considerable faith in the so-called "local treat-

ment" of women's disorders, illustrates the various sorts of sounds and applicators, and includes among his local treatment intra-uterine injections for endometritis, and electric vibration or electric massage.

In abdominal section he uses Trendelenburg's posture and varies the incision in accordance with the nature of the case. He differs radically from many American surgeons in his custom of leaving the abdominal cavity as dry as possible after operation. He makes no mention of introducing salt solution for absorption in the abdominal cavity. To prevent infection he surrounds the edges of the wound by large metal specula, which keep the abdomen open widely, and from the illustrations they should prove exceedingly useful. He would use drainage only in those cases where bacteria found in the abdomen are virulent, and where there is abundant material for their growth and nourishment. He endeavors to close the abdomen as soon as possible, believing that the admission of air for a long time may result in fresh bacterial invasion. The after-treatment which he advises is of the simplest variety. He allows the patient to get up early after operation, even in cases where the heart and bloodvessels are diseased. He uses salt solution freely by the bowel, and, if the patient goes on normally, removes the stitches in ten or twelve days. Vaginal puncture and incision, incision of the cervix and anterior vaginal hysterotomy are described and illustrated. He urges that a fair balance be struck between conservatism and the ambition to operate. The interests of the patient only must decide the choice of treatment.

In treating disorders of the external genital organs, he recognizes leukoplakia as a white thickening of the mucous membrane of the vulva, which is rightly termed kraurosis vulvæ when it surrounds the entire aperture. Laceration of the perineum is included in diseases of the external organs, and in complete lacerations he illustrates and practises the transverse flap method of Schröder. Under the head of diseases of the vagina he treats chorio-epithelioma, although this is almost invariably of uterine origin.

In endometritis, the subacute variety, he urges that care be exercised that no new infection be added, and that the physician wait until the infection has subsided, without sign of pelvic or abdominal involvement, before doing anything to the endometrium. Absolute rest and simple dietetic treatment are required in the first stages. In gonorrheal endometritis he would practise dilatation of the cervix after the initial stage had subsided, and the application of chloride of zinc to the interior of the uterus. Should the case prove obstinate, he would practically destroy the endometrium to prevent the recurrence of the infection. He would never practise curetting for catarrhal endometritis only, because of the presence of the discharge. He recognizes the protean character of endome-

tritis and its symptoms, and especially the pain which patients who suffer from this condition so frequently describe.

In the treatment of prolapse he describes plastic operations of the vagina, and illustrates them. There is nothing new in his methods. Amputation of the cervix rather than a conservative operation is recommended.

In treating myomata of the uterus, in some cases he prefers anterior hysterotomy and vaginal enucleation; in others the vaginal extirpation of the uterus is practised. Doyen's method of the abdominal extirpation of large tumors is illustrated and advised. It seems to him safer to remove the entire uterus where the tumor is of considerable size; where the tumor is small he operates through the vagina. In doubtful cases he prefers the upper operation, and tries, if possible, to leave at least one ovary in young women.

In treating cancer of the uterus, he employs formol solution on cotton to disinfect the vagina before operation. He has also had good results with vioform powder on gauze. He dissects away the the bladder from the uterus by the finger, and thinks it of great importance that this should be completely and carefully done. In most cases he operates through the vagina, closing the edges of the incision in the peritoneum as carefully as possible, and endeavoring to bring the peritoneum together over the upper end of the vaginal wound. He considers wounds and injuries to the bladder as among the most frequent accidents of the operation. He would also dissect out lymph glands as thoroughly as possible.

In discussing parametritis and perimetritis, he lays stress, as do most Germans, on treatment by baths and electricity, and especially electric baths in those cases of chronic parametritis which are not good subjects for operation. Ovariotomy is briefly but clearly described. He has occasionally removed ovarian tumors through the vagina. He would remove the Fallopian tubes in all cases of malignant disease where their condition is dangerous to the patient's life, and where there is reason to believe that serious disease would develop in the future. Where pus is found in both tubes, a radical abdominal operation is advised. In tuberculous cases he operates as little as possible, believing that general and dietetic treatments are preferable. A discussion of the diseases of the urinary passages closes the book.

In brief compass, 242 pages, Veit gives a clear and well-digested account of conservative gynecology at the present day. The book is valuable for its excellent balance, its clear and concise statements without padding, and may be taken as the mature expression of opinion of an intelligent observer. It is without bibliography, making no reference to other literature. Its illustrations are not abundant, but clear, and it is presented in the cheap paper binding, so commonly used upon the continent. E. P. D.

OLD AGE DEFERRED. THE CAUSES OF OLD AGE AND ITS POSTPONEMENT BY HYGIENIC AND THERAPEUTIC MEASURES. By ARNOLD LORAND, M.D. Second edition; translated, with additions by the Author, from the Third German Edition; pp. 472. Philadelphia: F. A. Davis Company, 1911.

IN a critique of Lorand's book one must bear in mind that the work has been written not only for the physician, but also for the layman (to whom, by the way, the publishers have freely advertised it). It is, therefore, not a scientific treatise on old age, but a charmingly personal series of "Plaudereien," in which sound common sense is found side by side with not a little exaggeration. The purpose of the book is to show the causes of psychical and physical decay, especially that coming on prematurely, and to indicate the ways in which the conditions characteristic of old age may be prevented or cured. Old age, in the author's opinion, is the result of disturbance in the function of the ductless glands, primarily the thyroid, but also the sexual glands, the pituitary body, the suprarenals, the pancreas, and the liver and kidney, which latter the author also includes among the ductless glands. There is hardly a disease which Lorand does not in some way connect with the thyroid. Old age he considers incomplete myxedema; indeed, one might say that the whole book is built around this particular thesis. He traces a strong connection between the thyroid and the sexual glands, and over and over again dwells on the apparent relation between markedly developed and long preserved sexual power and longevity. Like Sajous, whom he quotes freely, he holds that the opsonins are nothing more than thyroid secretion. Fever in infectious diseases is due to increased activity of the thyroid. Diminished activity of the thyroid predisposes to tuberculosis; a statement hardly consonant with the fact that in many cases of tuberculosis symptoms of hyperthyroidism are present. It follows quite naturally from the importance Lorand gives to the thyroid in pathological processes that he should look upon thyroid extract as almost a panacea. It is this advocacy of thyroid extract, and the stress laid upon the thyroid and other glands throughout the book, that the reviewer finds extravagant. For the sections dealing with diet, clothing, hygiene of the skin, and exercise, he has only praise. These chapters may be read with profit by physician and layman. While a teetotaler himself, not from principle but from distaste, Lorand is opposed to such narrowmindedness as prohibiting even the smallest amount of alcohol to those who only take it in the greatest moderation, solely on the ground that there are some good-for-nothings who can never take it without getting drunk. With regard to tobacco, he believes that two or three light cigars a day, never before meals, can do no harm save in exceptional cases. Though a bachelor, he nevertheless believes in the marriage state as a factor conducive to long life.

The author's knowledge of medical literature is vast; particularly gratifying are his abundant references to American writers. The references to German articles are often given in such a way that it is difficult to tell whether the paper referred to is German or Welsh. Stylistically, the book possesses a great deal of charm, and is characterized by a strong personal note, unusual in medical works.

D. R.

INTRODUCTION TO THERAPEUTIC INOCULATION. By CARMALT JONES, M.A., M.D., M.R.C.P., Assistant Physician and Director of the Department of Bacterio-Therapeutics, Westminster Hospital, London, England. Pp. 165; 11 illustrations, and 5 plates. London: Macmillan & Co., 1911.

THE contents of this little manual are divided into three parts, the first comprising 88 pages, dealing with the principles of inoculation therapy, with a short historical note; the second, of 41 pages, being a summary of methods and results obtained in the administration of vaccines; the last section, of 26 pages, being devoted to a detailed description of the technique employed in the preparation of the apparatus and in the making of vaccines and opsonic determinations.

This is the most satisfactory small treatise upon this subject that has yet appeared. It is distinguished by lucidity of expression and moderation of statement. Especially in the presentation of the results of treatment there is preserved a scientific poise which has been lacking in most publications by vaccine enthusiasts. The estimation of the opsonic index is commended both as an aid in diagnosis and as a control for therapeutic work but is conceded to be unnecessary for the clinician in many instances. A list, too long for enumeration, is given of diseases of the skin, the alimentary and intestinal tracts, of joints and bone, of lymphatic glands, of the genito-urinary tract, and of the eye and ear, and, in many, very considerable series of cases are adduced to show the expectation of cure or betterment under vaccine treatment. Much of the work is personal, but amplified by a few of the more reliable reports from the literature. One puts down the book feeling that in the birthplace of this method of treatment there has arrived a fair approximation of the value of this form of therapeusis, and that while hopes of miraculous cures are not justified in the majority of bacterial diseases, there yet exist good grounds for the employment of specific bacteriotherapy in infective conditions, particularly those of chronic and resistant nature.

D. B. P.

TEXT-BOOK OF MASSAGE. By L. L. DESPARD, Member and Examiner Incorporated Society of Trained Masseuses. Pp. 279; 203 illustrations, some colored. London: Oxford University Press, 1911.

MISS DESPARD has written with a lucidity and simplicity that suggests long and patient teaching. The abundant illustrations are well chosen. Much of the volume is given over to anatomy and physiology, but the remainder is mostly devoted to massage and considers the subject thoroughly as far as it goes. There is one matter of increasing importance which is neglected, and this is the treatment of tender areas that are so common in many parts of the body; they are usually called indurations, though familiarly known as "sore spots," and any statement which conveys the impression that such areas require gentle treatment is erroneous; their recognition and removal by the Swedish users of manual therapy is the one feature that makes theirs the system *par excellence;* for half a century the Swedes have written of these treatments, and for some years back the matter has been carefully considered in English literature, so that lack of knowledge upon this subject is hardly excusable.

Furthermore, it is to be regretted that some irregular practitioners have "discovered" these treatments and are employing the methods to their profit and to our chagrin; no other subject within the realm of manual therapy stands so urgently in need of widespread recognition. The book offers unusual aid in surgical conditions, and this is commendable. Since bandaging and electricity are considered, it appears that a section on mechanical vibratory massage would be germane to this work; however, this is unimportant, and the omission cited is the only just criticism to be offered against this excellent volume. N. S. Y.

HAY FEVER AND PAROXYSMAL SNEEZING. VASOMOTOR RHINITIS. By EUGENE S. YOUNG, M.D. (Edin.), Physician to the Manchester Hospital for Consumption and Diseases of the Throat. Pp. 147; 2 colored plates. New York: Wm. Wood & Co., 1910.

THIS is a well-written, instructive, and rather unusually accurate treatise on certain of the nasal neuroses. The book contains 147 pages, 85 of which are given up to the subject of hay fever, 35 to paroxysmal sneezing, and 7 to idiopathic rhinorrhea. The arrangement of the book is good, each of the subjects is dealt with in a systematic way, and there is a rather full general index. We are glad to see that the author has not omitted to put in references to

the literature that he has apparently read while reviewing the subject. It would have been better if the references had been indexed at the ends of the different chapters instead of at the bottom of each page, as they would then have been easier to consult. A rather disproportionally large part of the work is given up to the etiology of hay fever, and while he criticises fairly and in detail the different views and theories and gives with clearness the pros and cons of each, even after a careful reading, one is left with a great deal of uncertainty concerning the causation of the disease. As a matter of fact, this is at present about the extent of our knowledge concerning the etiology of hay fever. The treatment outlined is fairly extensive and seems to cover the whole field rather thoroughly. There is, however, an almost complete lack of detail concerning the various surgical procedures recommended, with the exception of the cutting of the nasal nerve and the removal of the tubercle of the septum, two operations which the author himself has devised, both of which seem to be still in the experimental stage. The illustrations are unimportant. On the whole, the book is a careful, well-written, up-to-date review of the subject with which it deals. G. B. W.

A Report on Hemoglobinuric Fever in the Canal Zone: A Study of its Etiology and Treatment. By W. E. Deeks, M.A., M.D., Chief of Medical Clinic, Ancon Hospital, C. Z., and W. M. James, M.D., Physician, Ancon Hospital. Pp. 177; 6 charts. Department of Sanitation: I. C. C. Press, Quartermaster's Department, Mount Hope, C. Z., 1911.

Of the publications following the increase of interest in black water fever which has succeeded upon the establishment of our modern knowledge of malaria, there are none within the knowledge of the writer which are of more importance to the subject than this monograph of Drs. Deeks and James. It is based upon the statistics of Ancon Hospital, running over the five years from September, 1905, to September, 1910, during which time more than 40,000 cases of malarial fever were dealt with in this institution, along with 230 cases of hemoglobinuric fever during the same period.

In their careful, logical, and complete analysis of the statistics before them, the authors point out that in the epidemiology of malaria and hemoglobinuric fever the periods of maximum intensity coincide; that hemoglobinuria as a whole prevails in direct proportion to the occurrence of malaria as a whole; that it prevails among a race in proportion to the susceptibility of that race to malaria and to the actual amount of such malarial infection in a given race; and that its prevalence bears no such relations with the prevalence of any other of the important infections met in the Canal Zone.

The authors are of opinion that in the Canal Zone (and inferentially elsewhere) hemoglobinuric fever has as its predisposing cause a prior malarial infection, that usually this is a prolonged or repeated infection, but that occasionally a single acute attack may induce this predisposition. They believe from the statistics which they employ that estivo-autumnal infection is particularly conducive to such a predisposition, and suggest that in part at least this fact may underlie the geographical discrepancies between the occurrence of malaria in general and hemoglobinuric fever. They acknowledge the probability of some unknown second factor operative as a determinant agent, and their records bear out the common contention that occasionally quinine may act as this second factor. They do not believe with Manson, Craig, and others that ordinarily this second factor is some unknown intercurrent infection, but suggest, in a theory which they propose, that it is some hemolysin developed and accumulated within the body of the subject in the previous period of the infection by the malarial hematozoa. This is the one weak part of the study, as is acknowledged by the writers, who, however, in academic argument, offer very rational grounds for not accepting Manson's surmises. Aside from this, no one may successfully cavil over the presentation made by Drs. Deeks and James. In the Canal Zone surely, and by inference anywhere else, hemoglobinuric fever is a manifestation of malaria; and it cannot be a misnomer to apply to it the old term of "malarial hemoglobinuria." But that the determining factor which acts in conjunction with the malarial predisposition is itself a product of the malarial infection, direct or indirect, is not proved. It is a permissible tentative assumption, to be verified or discarded when our knowledge is more advanced, just as the Mansonian idea of a complicating infection; and the writer feels that the study offered by Drs. Deek and James on the whole favors their inference.

Space does not permit one to present the discussion of this contention; but it is as easy to pick flaws and ask pertinent questions in regard to the theory of the authors as it is to deny the existence of a complicating hemolytic infection because it has not been demonstrated. There are analogies which are appealed to in support of the latter idea; in the history of Texas fever in cattle immune Southern cattle with Piroplasma bigeminum in their blood become hemoglobinuric when experimentally infected with rinderpest; and there is a growing feeling that the Anaplasma marginale found in the secondary access, when hemoglobinuria occurs, in cattle is not, as Smith and Kilbourne originally supposed, a phase of Piroplasma bigeminum, but in reality a second protozoan infection. Further study is essential, and this should not be limited to mere microscopic observation of the blood, but to bacterial culture from the blood, spleen, and allied organs as well. There are a number of arguments, for example, by which a second analogy could be erected

in the case of yellow fever, based on a view the writer has personally favored for a long time, by which the unknown protozoön of the disease is directly responsible only for the primary febrile access; and bacterial infection by bacillus x., Sanarelli's bacillus, or others of the so-called hemorrhagic group, enters secondarily to determine the secondary phenomena, including the jaundice, hemorrhage, and renal faults in which a fatal end is more common than in the primary phase. Hospital study would be more easy with a view of excluding such ideas than the experimental efforts necessary to prove the presence and malarial identity of a special hemolysin in cases of blackwater fever; and, it would appear to the writer, should be seriously considered by the Isthmian medical corps in continuance of the study which this work of Drs. Deeks and James so excellently summarizes and presents. Unquestionably these gentlemen and the general corps of Ancon Hospital, whose results they employ in their analytical study, have placed medical science under obligations to them; and the writer, in his partial hesitancy to follow them, by no means wishes to detract from the value of their work, but to suggest a line for future study with the view of verifying or correcting their present attitude. A. J. S.

DISEASES OF THE JOINTS AND SPINE. By HOWARD MARSH, M.A., M.C. (Cantab.), F.R.C.S., Master of Downing College and Professor of Surgery in the University of Cambridge, Consulting Surgeon to St. Bartholomew's Hospital, and to the Hospital for Sick Children, Great Ormond Street. New and enlarged edition, thoroughly revised by the author and by C. GORDON WATSON, F.R.C.S., Surgeon to the Metropolitan Hospital, Assistant Surgeon to St. Bartholomew's Hospital, etc. Pp. 632; 106 illustrations and 12 plates. Chicago: Chicago Medical Book Company, 1910.

THIS popular monograph appears in its third edition considerably enlarged, and presents in most sections the latest knowledge available on the subjects discussed. Over five hundred pages are devoted to diseases of the joints as such, and nearly one hundred to those of the spine.

Beginning with accounts of synovitis and injuries of the joints, the authors discuss in turn the general aspects of the acute arthritis of infants; of tuberculous, syphilitic, and gonorrheal arthritis; arthritis as seen in various infective diseases and septic arthritis; arthritis deformans, acute rheumatic arthritis, and arthritis in gout; "Charcot joints," joint changes in syringomyelia and hemophilia; newgrowths, cysts, and loose bodies in the joints; and ankylosis, with its treatment. The individual joints are next taken up in order; and Part I closes with chapters on congenital disloca-

tion of the hips, coxa vara, hysterical joints, interosseous pressure in joint disease, bone setting, movement, and massage.

In Part II, diseases of the spine, are discussed tuberculosis, malignant disease, spondylitis deformans, and necrotic spine.

Among the most interesting chapters are those dealing with infectious forms of arthritis. Though perhaps a clearer clinical distinction between infectious and dystrophic joint diseases could be drawn than has been done by the authors, their accounts of "subpyemic infections" are of great value; by this term they understand certain obscure pseudorheumatic joint lesions, seldom recognized, which resist all treatment until some source of toxin supply (dental caries, sinus disease, vaginal or uterine infection, etc.) is eliminated.

Of the dystrophic joint lesions, which they still confuse under the general term of arthritis deformans, they recognize two main classes —rheumatoid arthritis, in which synovial lesions predominate, and osteo-arthritis, in which bony lesions are conspicuous. Marsh and Watson seem not to have recognized as a distinct clinical and pathological entity the disease known in this country as the atrophic arthritis of Goldthwait and the metabolic osteo-arthritis of Nathan; yet certain features of their "rheumatoid arthritis" undoubtedly belong to this class, while others, which are confused with these, as surely belong among phenomena not of dystrophic but of infectious arthritis.

Apart from these questions of classification, which we believe could and should have been more satisfactorily solved, the volume affords the best guide to the pathology, diagnosis, and treatment of joint diseases at present to be secured in the English language in such compact form. A. P. C. A.

Taschenbuch der Pathologischen Anatomie. By Prof. Dr. Med. Edgar Gierke. I. Allgemeiner Teil; pp. 143; 69 illustrations. II. Spezieller Teil; pp. 207; 58 illustrations. Leipzig: Werner Klinkhardt., 1911.

This book is best described as an enlarged compend of pathology, covering the subject as usually taught in the medical school. It is intended to be used as an aid in taking accurate notes at lectures, and for this purpose wide margins have been left on each page. The text is usually concise, clear, and accurate, and the typographical work and illustrations are excellent. Although it is the intention of the author that the book shall supplement rather than supplant the lecture and text book of pathology, we feel that owing to its completeness it will tend to fulfil the latter purpose for many students, and hence the value of the book from a pedagogical standpoint is questionable. B. S. V.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Serum Treatment of Influenzal Meningitis.—WALLSTEIN (*Jour. Exper. Med.*, 1911, xiv, 73). Since more accurate studies on spinal fluid have been made, an increased number of cases of influenzal meningitis have been found, almost all of which have been fatal. Almost all cases are due to an influenzal bacteremia. The organism grows in the subdural space and is swept through the blood. The organism was cultivated on agar slants for twenty-four hours, then washed off with salt solution, and two such cultures, 2 c.c. in all, were injected into the canal of a monkey, giving a disease, fatal in thirty-six hours to four days, and comparable to that in man. A goat was now treated with living organisms for eighteen months, when opsonins and agglutinins appeared in his serum, but the serum is not bactericidal in vitro. This serum was effectual in securing recovery if injected into the spinal canal twenty-four hours after inoculation. The bacilli are more freely engulfed by the leukocytes, their growth and eruption into the blood hindered. To be successful in the human disease frequently repeated applications of the serum to the spinal canal will be necessary. The diagnosis can usually be made by immediate microscopic study of the fluid.

The Effect of Atropine on the Pulse during the Administration of Digitalis.—SELBERBERG (*Proc. Roy. Soc. Med.*, Lond., 1911, iv, 192) discusses the effect of atropine upon pulse rate in cases under treatment by digitalis. It is not yet definitely known how digitalis slows the heart, but it acts best on mitral cases of rheumatic origin that have developed auricular fibrillation and arrhythmia, while the senile type

of cardiac degeneration, those with a regular rhythm, and the tachycardia of fever do not respond so well. Lewis considers it due to a partial block, and that cases with a prolonged A-C interval, that is, with a delay in conductivity, will become slower on digitalis. But clinically, the cases with rapid irregular action, that is, with a short conduction time, become slower. Cushing thinks that digitalis increases inhibitory action of the vagus and prevents many impulses reaching the ventricle. Is the action mainly vagal, or are the conducting fibers of the auriculoventricular bundle themselves, or is the heart muscle lowered in irritability due to improved nutrition? In the senile type there is loss of inhibitory power of the vagus, and so atropine has little effect; also the cardiac musculature is so degenerated that nutrition cannot improve it much. By action of atropine the effects of vagus inhibition could be removed and so one of the possible factors would be cut out. The patient's pulse was studied at rest, under atropine alone, under digitalis, and under the drugs combined. It was found in the rheumatic cases with rapid heart that the rate was slowed by digitalis, and on administration of atropine, while the rate was increased, it in no case reached the original rate before drugs; if the effect had been due solely to vagal inhibition, it is fair to suppose that following atropine the old rate would have been reached. There are thus two component actions of digitalis, one vagal and the other on cardiac tissue, and they vary in different conditions. In the cases of auricular fibrillation that give high increases of pulse rate on the administration of atropine, digitalis works its best, for following digitalis atropine has almost no effect in raising the rate; that is, most of the effects of the digitalis are on the cardiac musculature. These cases, as a rule, do well and may even resume work again. By the study of pulse rates following atropine with and without digitalis, it is possible to find out whether digitalis is acting upon vagus or cardiac tissue.

Pathology of the Dyscrasic Edemas.—Débove (*Presse Méd.*, 1911, xix, 517). While edema due to mechanical cause has long been differentiated from that due to a chemical change in the blood, it is well to remember that the blood composition is kept constant by the kidneys. An excess of salt or water is quickly eliminated in health by the organs acting as a selective filter and removing the superabundant ingredient. But the excretion of a concentrated toxic fluid by the kidney may endanger the organ. So in the diseased body it is usual to find the superabundant toxins distributed not alone in the blood, but in the general body fluids. For example, if one ligates the ureters and then injects a rabbit with some dyestuff, this material will not be recoverable from the blood, but from the general body. As the toxins can only remain in the body fluid in solution, they are diluted and result in edema, which thus appears to be a defensive reaction against toxins, and preserves the chemical constitution of the blood intact. In typhoid fever and pneumonia, for example, the patient loses little in weight in spite of high fever, because of edema that is not recognizable because it is so general. In the diuresis of convalescence the toxins are rapidly poured out by the kidneys and weight is lost. This rapid outpouring of toxins could, in pneumonia, be spoken of as a chloruria, because chlorides had been retained to make the toxic solution physiologically

normal and are now excreted rapidly. Not only does edema save the kidney from excreting too highly toxic fluids, but as antibodies are present in all transudates, the toxins are catabolized in the tissues and so rendered innocuous. Probably the pathogenesis of edema is the same in nephritis. Nephritis is largely due to a hematogenic infection. Frequently the fact is overlooked that the causative agent persists even if the kidney lesion makes no progress. Here the organism protects itself from the assault by edema in hydropic nephritis and by polyuria in the anhydropic. Clinically, in the hydropic form, it has been observed that a disappearance of edema has been followed by an exacerbation of the symptoms caused originally by the toxins, a fact that can be explained only by supposing the elimination of a too highly concentrated urine. But while Widal and Javal believe the edema of nephritis to be due to a primary retention of chlorides through kidney impermeability, Débove thinks it a primary retention of toxins. The blood and lymph contain the same amounts of chlorides before, during, and after nephritis, and it is highly probable that water and salts are retained to make the toxins dilute enough, also isotonic. When salt is excluded from the diet the edema is reabsorbed and gradually excreted. Sodium chloride is one of the simplest things for the kidney to excrete in health. In disease this power is somewhat impaired, but by no means so much as is the power of urea excretion. He thinks of flooding the kidney with a highly toxic urine. In this toxicity there is no reason to believe that sodium chloride plays any important part. In the interstitial form the organism tries to secure elimination by polyuria because the toxins are different and have acted upon different kidney structures. While many types of edema are mechanical in origin, we cannot afford to overlook the primary chemical change in the blood as is found in cirrhosis of the liver.

Functional Diagnosis of the Liver.—F. Falk and P. Saxl (*Zeit. f. klin. Med.*, 1911, lxxiii, 131) point to the fact that while amino-acids have frequently been found in the urine in large quantity in hepatic disease, practically no attention has been paid to the occurrence of the more complex nitrogenous bodies (polypeptids). The authors, therefore, undertook a study of the amount of amino-acid nitrogen and of peptid nitrogen in cases of primary liver disease and also in cases where the liver was affected secondarily. To determine the peptid N, they used the formalin titration method of Sörensen. As Falk and Saxl have previously shown, this method, as modified slightly by them, gives results which, though not absolute, are sufficiently accurate for clinical purposes. The studies of Falk and Saxl show that hepatic disease in general causes an increase in the relative quantity of both the amino-acid and the peptid N. Ordinarily the two are increased proportionally, but exceptions to this are quite frequent. After feeding glycocoll, they find no changes in the nitrogenous fractions in patients with normal livers; with hepatic disease, and particularly cirrhosis, they observed a great increase in the peptid N fraction.

The Blood Findings in Epidemic Cerebrospinal Meningitis.—Rusca (*Deut. Archiv f. klin. Med.*, 1911, ciii, 235) has made a rather complete study of the blood in nine cases of epidemic cerebrospinal meningitis,

of which six were fatal. At the beginning of the disease there is a leukocytosis, due mainly to an increase in the number of the polynuclear neutrophilic cells; the lymphocytes may be slightly increased or decreased. During the course of the disease, there occurs with each aggravation of the symptoms both a relative and an absolute increase of the polynuclear neutrophiles. During the decline of the acute symptoms there is a corresponding drop in the relative and absolute number of these cells. Thus, if one plots the lymphocyte and polynuclear neutrophile curves, it is found that they diverge with a recrudescence and tend to become approximated during recovery. In the cured cases, Rusca found a crossing of the polynuclear neutrophilic and lymphocytic curves, the lymphocytes becoming more numerous. Following a simple lumbar puncture, the author observed a fall in the leukocyte count. This fact should be remembered in those cases treated with serum, lest a similar occurrence should be attributed to the serum. In 2 of the cases which recovered, the eosinophiles were greatly increased, both absolutely and relatively. Mastzellen were lacking in all the fatal cases shortly before death. In 4 of his cases the author saw the meningococcus in the stained blood film, and in one of these a blood culture made immediately after studying the film yielded a positive culture.

Colloidal Nitrogen in the Urine in Cancer.—S. MANCINI (*Deut. Archiv f. klin. Med.*, 1911, ciii, 288) has examined the urine for colloidal nitrogen according to the method of Salkowski. The twenty-four-hour specimen was always used. When alkaline in reaction, the urine was acidified slightly with acetic acid. Albumin, when present, was removed before examining for the colloidal nitrogen. The percentage of colloidal nitrogen in normal urine, taking the total nitrogen as 100 per cent., is about 3.56, according to Salkowski. Mancini found an increase of the colloidal nitrogen in cancer, the average being 6.48 per cent. of total N. He finds, however, that this increase is not specific for the urine in cancer, since a similar result may be encountered in pneumonia and pleurisy as well. Indeed, there may be an increase in all those diseases in which there is a continuous absorption of exudates or transudates, such as pneumonia, pleurisy, anasarca from whatever cause, cirrhosis of the liver, and purulent processes. An abnormally large proportion of colloidal nitrogen is, therefore, not diagnostic of cancer, but it may be of great aid in arriving at the correct diagnosis.

Irregularity of Feeding and its Effect on the Stomach.—KÜLBS (*Ztschr. f. klin. Med.*, 1911, lxxiii, 47) studied experimentally the effects of irregularity in feeding and also the time intervals between feedings which may be endured without loss in weight. The experiments were all carried out upon cats, and Külbs believes his findings may have some bearing on human pathology. The results he obtained are as follows: (1) If one gives a cat as much meat daily as it cares for, the animal soon regulates the quantity consumed, avoiding an excess. (2) Animals fed every second, third, or fourth day eat rather less that two-, three-, or fourfold the quantity of a daily ration. They do not lose weight, however, so long as they are fed regularly. (3) Slight irregularities in the time of feeding cause no disturbances. (4)

If the feeding hours are very irregular, death frequently follows with rapid loss in body weight. There is found a greatly dilated stomach or, less often, a subacute gastro-enteritis. (5) Occasionally, when the animals are fed regularly at long intervals, they die with atony of the stomach and rapid emaciation. (6) These observations may, perhaps, be correlated with the fact observed in man that the human stomach is frequently upset when the meals are taken at very irregular intervals.

The Diagnostic Value of Diastase in the Urine. — E. MARINO (*Deut. Archiv f. klin. Med.*, 1911, ciii, 326) reports a quantitative study of urinary diastase in various diseases. He used the method of Wohlgemuth. The author finds (1) that the excretion of diastase in the urine is greatly lessened in nephritis and in diabetes mellitus. (3) In pancreatic disease the urinary diastase is increased in quantity. This, the author believes, is a very important sign of pancreatic disease. (3) As a functional test of the kidney, the quantitative estimation of diastase is valuable. (4) In pernicious anemia and in secondary anemia the diastase of the urine is markedly decreased. The diminution seems to be greater in pernicious than in secondary anemia, though the number of cases studied was too small to formulate a rule.

The Rate of Regeneration of Blood Platelets.—W. W. DUKE (*Jour. Exper. Med.*, 1911, xiv, 265) has been able to render the blood of dogs practically free of platelets by withdrawing 200 to 300 c.c. of blood from the carotid artery, defibrinating it completely, and then reinjecting it intravenously. A repetition of this procedure six to ten times reduces the number of platelets to a minimum. He finds that animals thus deprived of the greater part of their fibrinogen and platelets display a marked tendency to bleed. After the practical removal of platelets from the blood, their regeneration is very rapid, amounting to about one-fifth of the normal number daily. From observations on human beings, Duke believes that the life cycle of the platelets is a matter of only a few days.

The Production, Life, and Death of Crescents in Malignant Tertian Malaria.—D. THOMSON (*Annals Trop. Med. and Parasitol.*, 1911, v, 57) has studied the production, life, and death of crescents in treated and untreated cases of malignant tertian malaria by means of an enumerative method, the details of which are to be given in a forthcoming report. His results are summarized as follows: (1) Crescents are produced from the ordinary asexual spores of *P. falciparum*, due to a development of immunity toward the latter. (2) They develop somewhere in the internal organs and then appear suddenly in the peripheral blood. (3) The period required for their development is about ten days. (4) Crescents do not generally live more than a few days in the peripheral blood. (5) Crescents may be present in the peripheral blood during periods as long as eight weeks, not because the individual crescents survive for that time, but because their numbers are constantly replenished from surviving asexual forms. (6) Fresh broods of crescents come into the circulating blood daily, or every other day, or irregularly, according as the asexual sporulations occurring ten days before were quotidian, tertian, or irregular. (7) Quinine

has no direct destructive action on crescents, either during their development or afterward, but it destroys the asexual source of supply. (8) Quinine reduced the crescents to numbers less than 1 per c.mm. of blood within three weeks, provided it be given in daily doses of 20 to 30 grains. (9) Quinine in small doses tends to increase the crescent production (?) by favoring the development of immunity to the asexual parasites. (10) Methylene blue in doses of 12 grains daily reduces the number of crescents, and would seem to have some direct destructive action upon them.

Antityphoid Vaccination in the Army.—J. R. KEAN (*Jour. Amer. Med. Assoc.*, 1911, lvii, 713) reports the wonderful sanitary record of the Maneuver Division of the Army at San Antonio, and compares the statistics with those of one of the camps in 1898. The most important features of his report deals with typhoid fever prophylaxis by means of typhoid vaccine. Eight thousand and ninety-seven men were vaccinated. In no case was the operation followed by serious results, and in 90 per cent. of the cases the reaction was mild or absent. In the entire division there was only one case of typhoid fever. "This patient, a private in the hospital corps, had not completed his immunization, having taken only two doses. The case was very mild, and would perhaps have been overlooked but for the rule that blood cultures were made in all cases of fever of over forty-eight hours' duration." During the time covered by this report 49 cases of typhoid fever, with 19 deaths, were reported in the city of San Antonio. Compared with the typhoid morbidity and mortality at Jacksonville, Fla., in 1898, the results at San Antonio show the extent of the advance. In Jacksonville, among 10,759 men, there were 1729 certain cases of typhoid fever (including the probable cases of typhoid, there were 2693), of which 248 resulted fatally.

The Leukocytes in Malaria: A Method of Diagnosticating Malaria Long after it is Apparently Cured.—D. THOMSON (*Annals Trop. Med. and Parasitol.*, 1911, v, 83) has made many daily observations of the total and relative leukocyte counts in malaria, extending over long periods of time and after the patients were apparently cured. His findings are remarkable and unique. They are accompanied by numerous charts. The summary, in Thomson's own words, follows: (1) During active malaria the number of leukocytes in the peripheral blood is decreased. During quiescent malaria, and in cases apparently cured by treatment, the leukocytes in the peripheral blood are much increased. (2) During the rigor and temperature in malaria the mononuclear leukocyte percentage (more especially that of the large mononucleated variety) is low. With the fall in temperature, however, the mononuclear percentage rises very high, sometimes even to 90 per cent. of the total leukocytes. This fluctuation in the percentage of total mononuclear leukocytes occurs also long after continuous quinine treatment, and is observed for months and even years (?) after the last attack of fever. (3) In these apparently cured cases of malaria the mononuclear percentage is lowest at the time of the day at which the rigor and fever occurred during the previous active malaria; and, moreover, at this time there also occurs a very marked leukocytosis, which continues only for a few hours. The leukocytes reach numbers

as great as 30,000 to 50,000 per c.mm. of blood. On one occasion they were as numerous as 125,000 per c.mm. Two hours later they had fallen to 22,000 per c.mm., and in eight more hours they were only 6000 per c.mm. This case showed a regular daily periodic variation in the number of leukocytes, averaging from about 6000 per c.mm. to 50,000 per c.mm. The height of the rise always occurred about noon. This was the time at which the rigor and fever, which was quotidian, were wont to occur previously. This postmalarial leukocyte phenomenon occurred always without exception in the 40 cases examined, and would therefore seem to be an infallible sign of previous malaria, as, so far, it has not been observed in any other disease. (4) It would appear that large numbers of malarial parasites on sporulating cause a leukopenia, while a very small number on sporulating cause a leukocytosis.

Albumin and Albumose in the Sputum.—E. H. GOODMAN (*Archiv. Int. Med.*, 1911, viii, 163) has studied the albumin and albumose content of the sputum in a number of pulmonary diseases, and finds that the presence of albumin is of less diagnostic value than is attributed to it by certain observers. While albumin is usually present in the sputum in pulmonary tuberculosis and absent in simple bronchitis, exceptions are so frequent as to destroy the value of the test to a great extent. In fact, Goodman met with albumin frequently in non-tuberculous cases. He finds in most cases that the albumin is associated with a positive test for occult blood which probably explains the source of the albumin.

SURGERY

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Experimental and Clinical Investigations Concerning the Effect of Fibrolysins on Cicatricial Tissue.—SIDORENKO (*Deutsch. Ztschr. f. Chir.*, 1911, cx, 89) says that in the last five or six years contributions have frequently been made concerning the favorable action of thiosinamin and its derivatives. Sidorenko made investigations to determine the value of thiosinamin-fibrolysin therapy. Clinically the fibrolysin was employed in a series of suitable cases. In the laboratory the effects of the fibrolysins were investigated upon cicatricial tissue, the blood, and the lymph taken from the thoracic duct. The experiments

were made on dogs, rabbits, and white mice. In the histological preparations no effect whatever of the fibrolysins could be found. The lymphogogue effect of the fibrolysin is at the present time doubtful. From the fluctuation in the number of leukocytes found, the fibrolysin is not shown to be a specific means of producing a leukocytosis. The therapeutic dose is harmless and produces no favorable appearances. From a critical examination of the material of other authors and of his own, the clinical and experimental evidence allows the assertion to be made that fibrolysins do not exert a therapeutic effect upon cicatricial tissue.

Thrombosis of the Cavernous Sinus not of Otitic Origin.—Otto (*Deut. Ztschr. f. Chir.*, 1911, cx, 177) says that thrombosis of the lateral sinus is frequently of otitic origin, and rarely arises from a surface infection with a thrombophlebitis progressing into the cranial cavity. He reports a case in which a carbuncle of the back of the neck gave rise to a septic thrombosis of the cavernous sinus which was demonstrated at autopsy. From his study of the subject he concludes that the cause of the thrombosis of the lateral sinus is infectious in most cases. Alveolar periostitis and erysipelas play a conspicuous role in the etiology. Carbuncle of the back of the neck is a rare cause. The symptoms, besides those of general sepsis and those due to the causal disease, are the results of disturbances in the circulation of the sinus, rarely unilateral, since the thrombosis soon extends to the other side. For the diagnosis, of chief importance are: The eye symptoms (exophthalmos, chemosis, paralysis of the eye muscles, especially ptosis, changes in the eye grounds from stasis), with pyemic temperature. Thrombosis of the cavernous sinus can be assumed as certain, when these eye symptoms are bilateral. An infectious thrombosis of the cavernous sinus is a disease which almost always runs a fatal course, although spontaneous healing does occur. A prospect of saving the patient's life is offered by early operation, which should aim at emptying the sinus itself. Because of the difficulty of gaining access to the sinus, one should be very cautious in its performance.

Pyloric Stenosis in Infancy.—Richter (*Surg., Gyn., and Obst.*, 1911, xii, 568) says that it is evident that the abundant literature on the subject that has developed in the last ten years is resulting in the recognition of this disease as a widely distributed condition. Two types are generally recognized—one characterized by a spasmodic action of the normal or slightly hypertrophied pyloric musculature, the other by an hypertrophy of the circular muscle of the pylorus, which enlarges to such an extent as to produce a tumor mass which effectually blocks the pyloric lumen, causing a mechanical obstruction. Richter uses the term "pyloric stenosis in infancy" in a general sense to include all cases; and limits the terms "spasm" and "hypertrophy" to the above-described conditions. The symptoms begin during the first weeks of life, usually in the second, third, or fourth. The first symptoms to attract attention are vomiting, constipation, and loss of weight. The vomiting is of a peculiar propulsive type. In one case the vomitus was thrown a distance of four feet. Vomiting commonly is accompanied by diarrhea. In pyloric obstruction it is accompanied by constipation.

With the vomiting and constipation are all the usual accompanying evidences of mechanical obstruction found in the adult—rapid loss of weight, profound depression, though not suggestive of the collapse of gangrene. With the diminished ingestion of fluids the baby presents the shrunken appearance of excessive dehydration. The urine is greatly diminished and finally almost totally suppressed. The upper abdomen is full, tense, and bulging, and is made more prominent by a marked retraction in the hypogastric region. The bulging mass is due to the distended stomach, made more evident by the collapsed and empty state of the bowels. In cases with hypertrophy, there can be palpated a small, solid, and very freely movable tumor, above and to the right of the umbilicus. Three types of operation have been widely practised—division of the pylorus, pyloroplasty, and gastro-enterostomy. Gastro-enterostomy has been the operation of choice of the great majority of operators, and was performed in the eleven cases operated on by Richter. There was one operative death, and of the 10 cases that recovered, one has since died. It was a typical hypertrophic stenosis. There is a universal gain in weight following the operation. None of the nine babies living shows any evidence of intestinal disturbance.

Concerning the Behavior of the Intestine under the Influence of the Digestive Activity of the Gastric Juice.—Fiori (*Zentralbl. f. Chir.*, 1911, xxxiii, 890) conducted a series of experiments on cats and dogs to show that the jejunal wall is not damaged in any way by contact with the gastric juice. He believes that the tissues of the intestinal wall contain an antiferment, which is capable of resisting the proteolytic action of the pepsin. The first series of experiments consisted in simply attaching the intestine to the stomach by a continuous seroserous suture, without opening the stomach. In the second series, a portion of the intestinal loop was laid in the thickness of the stomach wall between the mucosa and muscularis, without opening the stomach. In the third series the same operation was performed as in the second, with excision of the muscular layer around the attached portion of the intestine. In the fourth series the intestine was attached to the stomach as in the first series, but the stomach was then opened and the stomach wall was then excised at the site of the attachment of the intestine. This was to insure against the constriction of the intestinal wall by the muscular ring in the stomach wall. In the fifth series an excised portion of the small or large intestine, with good vascularity, was laid in a corresponding deficiency in the stomach wall. In none of the seven dogs operated on in the last series, which lived from two to thirty-six days after operation, was any change observed in the transplanted piece of intestine. This was a positive proof of the resistance of the intestine against the digestive activity of the gastric juice. While in the first series no disturbances arose from the simple attachment of the intestine to the stomach by the continuous seroserous suture, in the second and third series it was shown that the gastric muscle surrounding the attached intestinal loop can cause severe disturbances of nutrition, which may lead to necrosis of the tissues enclosed. In the fourth series it was shown that the intestinal wall, when not under the ischemizing influence of the gastric muscle ring, can resist the digestive

influence of the gastric juice. As the result of a long series of chemico-physiological experiments, Fiori believes that there exists in the intestinal mucosa, as in that of the stomach, an antiproteolytic substance.

The Care of the Stump after Resection of the Stomach.—Polya (*Zentral. f. Chir.*, 1911, xxxviii, 892) says that of the various methods of treating the gastric and duodenal stumps after resection of the stomach, that of Kocher more than any other restores the normal anatomical conditions. Yet after an extensive resection with the best possible mobilization of the duodenum, the gastroduodenostomy can not be performed without tension, and this leads easily to suture insufficiency. When the gastric stump is too small and the anastomosis opening is placed in the posterior wall of the stomach close to the occlusion sutures, the intervening strip of stomach wall may necrose, as has been observed several times. In the Billroth I operation the danger of suture insufficiency is still greater. In the Billroth II operation regurgitation threatens, especially when the gastric stump is too small to permit a gastro-enterostomy opening of suitable size and position. The operation which Polya employs for exhaustive stomach resections where the Kocher method cannot be performed easily and without tension consists briefly in implanting the gastric stump in its whole extent, end to side, into a longitudinal opening in the upper loop of the jejunum, which is brought through the opening in the mesocolon. The advantages are as follows: The gastro-enterostomy is easily performed, and the gastric stump can be united to the intestine without any tension. The suture holds very securely and brings together in all parts broad serous surfaces. The most favorable conditions are provided for the emptying of the stomach contents, the communicating opening is very wide, is at the aboral end of the gastric stump, and provides a physiological direction for the passage of the stomach contents. The stomach discharges its contents into the upper part of the jejunum, so that there is no afferent loop, as is the case in Mayo's no loop gastro-enterostomy. The suture for closing the end of the gastric stump is avoided. Polya has performed the operation on 6 patients with extensive resections of the stomach for cancer. Two patients left the hospital cured. One seventy-year-old patient was completely well in five weeks, except for a small fistula which kept her in the hospital. Then erysipelas developed on the nose and extended over the whole scalp, and finally infected the small abdominal fistula. The patient died forty-nine days after operation with an acute retroperitoneal phlegmon. Three very severe cases which died one to two days after operation showed that the gastro-enterostomies healed without fault.

The Employment of a 1 Per Cent. Camphorated Oil in Peritonitis and its Effect in Preventing Adhesion Formation.—Hirschel (*Zentralbl. f. Chir.*, 1911, xxxviii, 1022) says that he was the first to employ camphorated oil for the treatment of the inflamed peritoneum in man, which he did in 1907. Others followed, some, especially the gynecologists using it not for peritonitis but as a preventive of it. It was then injected into the abdominal cavity forty-eight hours before the operation to increase the resistance of the peritoneum. Hirschel employs it only in very bad cases of peritonitis, mostly after per-

foration of the appendix, but also after perforations of the stomach and intestines. The purpose of this paper was to repeat briefly the technique which he follows. Every operation for diffuse peritonitis should be done as quickly and with as little interference as possible. The pus is best removed from the peritoneal cavity with dry or moist gauze pads as thoroughly as possible, although the peritoneum cannot be completely cleansed. The pus must be taken up on both sides, when necessary in the upper part of the abdomen, and especially in the pouch of Douglas. With a gauze pad on a long holder the warm 1 per cent. camphorated oil is spread over the whole abdominal cavity in excessive quantity, on the parietal and visceral surfaces and between the coils of intestine, so that all the serous surfaces are glossed with it. It may be poured into Douglas' pouch. The quantity used may be 200 to 300 grams. The abdominal wound is then closed to the drainage tube. The focus of the peritonitis must, of course, always be removed or rendered harmless. The camphor stimulates the heart, and this effect lasts a long time. The paralyzed intestine soon shows peristalsis, and soon after the operation gas is passed by the rectum. The frequent vomiting observed before the operation, ceases immediately. In one case, in which long after the introduction of the oil a complication led to a fatal termination, at the autopsy there was found everywhere a very smooth peritoneum which was covered with a fine layer of oil. No kinking or strong adhesions could be found. In one case, in which the oil had been employed for a diffuse peritonitis, several months later operation was necessary for an abdominal hernia. Except for one small omental adhesion to the scar, no further adhesions were found.

Extraperitoneal Embedding of the Omentum in the Kidney as a Therapeutic Measure, Especially as a Diuretic. — TORIKATA (*Deut. Ztschr. f. Chir.*, 1911, cx, 420) says that Bakes, in 1904, was the first to wrap with omentum the denuded kidney extraperitoneally, in a case of nephritis. Phocas decapsulated the kidney for ascites from liver cirrhosis, because he had observed that this operation, when done for nephritis (Edebohls), had a strong diuretic effect. Omi, in 1907, among other experiments on dogs, placed the left kidney intraperitoneally, fixed the omentum by sutures in a wound of the kidney, and showed that an excellent venous anastomosis could be obtained in this way. Isobe recently studied intraperitoneal omental embedding in the kidney, and came to the conclusion that this operation gave the best results up to the present time with relation to anastomosis formation, venous as well as arterial. Torikata recently treated a case of ascites with anasarca, by embedding the omentum in the kidney in its extraperitoneal position. After a study of the subject, he concludes that for anasarca from nephritis, when operative treatment is to be considered, extraperitoneal embedding of the omentum in the kidney is a better operation than the denudation or the surrounding of the kidney with omentum. In combating ascites from portal obstruction, most surgeons prefer the operation of omentopexy to the anterior abdominal wall. Torikata recommends very strongly his operation, which includes an omentopexy, and in addition has a diuretic effect. Finally, he concludes that his operation deserves undoubtedly the preference when hepatic cirrhosis and nephritis are combined in the same patient.

The Ideal Operation for Arterial Aneurysm; A Contribution to the Circular Suture of Vessels in Man.—Omi (*Deut. Ztschr. f. Chir*, 1911, cx, 443) operated on a case of popliteal aneurysm as follows: Under chloroform narcosis and with the limb rendered bloodless by an Esmarch tourniquet, an incision was made about 20 cm. long over the tumor. The aneurysm was isolated with little difficulty. The popliteal artery entered and emerged on the medial side of the sac. This was then opened and a large quantity of clotted and fluid blood escaped. The sac was extirpated as a whole with a short piece of the afferent and of the efferent portion of the artery, so that 4 cm. of the artery was removed. The popliteal vein lay external to the artery without a communication between them. After the application of forceps the tourniquet was removed. The two arterial stumps could be brought together easily by flexing the knee, and they were united by a Carrel-stitch circular suture. The arterial wall was markedly thickened and sclerosed, so that suturing with a fine needle was difficult. Before drying, the site of operation was protected by dropping on it repeatedly Lock's solution. After removal of the forceps and digital compression for a few minutes, no signs of hemorrhage from the suture holes could be seen. The wound was closed except for a gauze drain. The popliteal artery pulsated distinctly and the pulsation in the dorsalis pedis and posterior tibial were unchanged and the tissues everywhere were warm. The limb was fixed in the flexed position. On the next day pulsation could be felt in the posterior tibial and on the second day in the dorsalis pedis. Ten days after the operation the wound was healed and then the limb was gradually extended. On the twenty-first day the patient went about with crutches. Thirty days after the operation, pulsation in the posterior tibial and dorsalis pedis could be detected. The patient now walks without difficulty.

The Storing of Blood in the Extremities, its Influence on the Bleeding in Operations, and its Effect upon the Organism.—Zoeppritz (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1911, xxiii, 367) says it was known to the ancients that blood could be stored up in the extremities by applying a tourniquet near the trunk, and this method was employed for arresting hemorrhage especially from the lungs. They also recognized that it was not without danger. The method was also employed for hemorrhage from the nose, and in the last twenty years the indications have been extended to combating edema of the lungs, apoplexy, and disturbances of the circulation calling for blood letting. The tourniquet should be applied as close as possible to the trunk and with moderate tension, so as to occlude the veins with as little interference as possible with the arteries. In a muscular thigh it is often difficult to regulate the pressure, but it is more simple in the arm. The pulsation in the dorsalis pedis artery in the lower extremity, and in the radial in the upper extremity, can be felt at first, but in about ten minutes it cannot because of the complete stoppage of the venous current. After some time the early redness turns to a dark blue color, so that one is tempted to remove the tourniquet. But this should not be done. It is necessary to guard against too great loss of heat in the limb by wrapping it up well. From an extensive study of the subject, Zoeppritz concludes that by applying a tourniquet to the roots of the extremities by a suit-

able technique, about one-fourth of the total blood of the body can be stored in the extremities. To this bleeding into the extremities the body answers with more or less diminution of the blood pressure, increased frequency of the pulse, and disturbance of the breathing. The method may be employed as a prophylactic against hemorrhage during operations. It is to be recommended in operations on the brain, when there is no increase of the intracranial pressure, in operations on the spinal cord, and in other operations when severe parenchymatous bleeding is expected. There is no danger of a secondary hemorrhage. Some of the contraindications are brain pressure, arteriosclerosis, blood diseases, varicose veins, etc. The maximum of stored blood in the extremities, with a proper technique, is obtained on an average after one and one-half hours. A diminution of the force of the heart beat is to be recognized by the pulse after a long-continued application of the tourniquet, and an increase of the same on releasing the tourniquet. With the brain exposed, on releasing the tourniquet, the whole brain mass rises, and the pulsation is well established.

Concerning the Late Effects of Chloroform Narcosis. — STIERLIN (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1911, xxiii, 408) says that while the dangers of chloroform narcosis are usually over with on the first signs of returning consciousness, this rule is not without exception. Fortunately the cases are rare in which, from one to several days later, threatening and usually fatal conditions arise, for which the chloroform is responsible. The results of investigations do not justify us in ignoring the existence of a permanent idiosyncrasy against chloroform poisoning, for in individual cases it may be of very great importance. It has been shown that such an idiosyncrasy may be transitory or may be due to a diminished resistance, as from certain diseased conditions. Such conditions are septic or suppurative processes, cases of autointoxication, principally in connection with torsions, strangulations, and incarcerations of abdominal organs (twisting of pedicles of ovarian cysts, volvulus, obstructed herniæ, omental or mesenteric cysts). The danger of chloroform in these affections increases with the intensity and duration of the narcosis, and most likely with the size of the twisted organ or strangulated portion of intestine, and is less with a brief, uncomplicated incarcerated hernia. The danger, however, is always so great that chloroform narcosis is very strictly contraindicated in all the above conditions and in pyosalpinx. In such cases the quantity of chloroform which would be borne by some men and many other patients without difficulty, would be sufficient to cause severe damage to the liver and kidneys, and subsequently the death of the patient. The causes of the decreased resistance to chloroform are to be found probably, partly in autolytic changes or abnormal internal secretions, which can aid the narcotic poison; partly in a previously existing degree of liver insufficiency, which from the effect of the narcotic may cause a deleterious accumulation.

The Motor Function of the Pyloric Sphincter and Pyloric Antrum in Dogs after a Transverse Division of the Stomach. — KIRSCHNER and MANGOLD (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1911, xxiii, 446) found, after complete transverse division of the stomach in dogs,

thus separating the pyloric half from the influences of the vagus nerve and from its functional relationship with the cardiac half, that the tone of the pyloric sphincter and the rythm of the change between its closure and opening during the emptying of the stomach is completely normal. The increase in pressure due to contraction of the pyloric antrum, the rhythm, and the character of the antrum contraction remain unchanged. The functional coördination of the sphincter and antrum of the pylorus is preserved. The chemoreflex of the pyloric portion of the stomach, beginning in the duodenal mucus membrane, continues. Since the physiology of the dog's stomach is very much the same as that of the human stomach, we are justified in transferring the knowledge obtained in dogs to the human, where the clinical observations up to the present time do not contradict the results obtained in dogs. It is a striking fact that, as already mentioned, apparently normal stomach function is reëstablished very soon after the operation of tranverse resection of the stomach. This transverse resection with immediate union of the wound surfaces has not only the advantage of restoring the normal anatomical relations as much as possible, but it brings about a complete restoration of the physiological relations, since the regulative and motor functions of the distal portion of the stomach are not disturbed. To what degree pathological conditions of the sphincter and antrum of the pylorus, such as motor sluggishness or increased tone (pyloric spasm), existing before the operation, will be influenced by transverse division of the stomach cannot be determined by the results of the writers' experiments.

The Control of Bleeding in Operations for Brain Tumors.—CUSHING (*Annals of Surgery*, 1911, liv, 1) says that one of the chief objects of concern in intracranial surgery should be the avoidance of any unnecessary loss of blood, for at best, in many cases of brain tumor associated with venous stasis, bleeding is likely to be so excessive as to necessitate postponement of the final steps of the procedure until a second or even a third session. The common methods of stilling blood by sponge, clamp, and ligature are largely inapplicable to intracranial surgery, particularly in the presence of bleeding from the nervous tissues themselves, and any device which serves as an aid to hemostasis in these difficult operations will bring a larger number of them to a safe termination at a single sitting, with less loss of blood and less damage to the brain itself. In addition to the more familiar tourniquet for the scalp, and wax for diploetic and emissary bleeding, suggestions are offered as to the use of gauze pledgets, dry sterile cotton, fragments of raw muscle and other tissues, as well as sections of organized blood clots for superficial meningeal bleeding, and silver "clips" for inaccessible individual points either in dura or brain. The successful consummation of any critical operation often depends upon seeming trifles. It is, however, the scrupulous observance of surgical minutiæ that makes possible the safe conduct of major intracranial performances.

THERAPEUTICS

UNDER THE CHARGE OF

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Influenzal Meningitis and its Serum Treatment.—FLEXNER (*Jour. Amer. Med. Assoc.*, 1911, lvii, 16) says that influenzal meningitis can no longer be considered a rare disease. Within a few months, in the United States alone, reports dealing with this subject have been published by Wollstein, Dunn, and Davis. All but 6 of the 58 cases thus far reported have terminated fatally. Wollstein has been able to induce in monkeys a severe form of cerebrospinal meningitis by the injection into the spinal canal of virulent cultures of influenza bacilli. An immune serum was then prepared from goats by repeated injections of virulent influenza bacilli extending over a long period of time. It has been found possible to rescue monkeys regularly from the fatal effects of the subdural inoculation of cultures of the influenza bacillus, through daily injection, by means of lumbar puncture, of the immune serum for three or four days. Flexner advises this treatment for influenzal meningitis in human beings in the same manner in which the serum for epidemic meningitis is employed.

The Present Status of Diabetes Mellitus.—MINKOWSKI (*Med. Klin.*, 1911, vii, 1031) believes that the oatmeal cure is only suited to individual cases of diabetes and that the benefit derived from its use is often not permanent. However, he has seen remarkable results by this method and he does not hesitate to recommend it, especially for the severe type of the disease. He is of the opinion that the beneficial results obtained by the oatmeal treatment are due in part to the restriction of the protein intake. The restriction of the proteins in the diet reduces the metabolism as a whole and also eliminates them as a source of sugar production. He quotes Naunyn, who appreciated the importance of reducing the total metabolic processes in diabetes in order to secure a minimum excretion of glucose. For this reason, Minkowski thinks that it is wise to reduce the amount of muscular exercise in severe cases of diabetes. He also believes that the former strict withdrawal of carbohydrates in the treatment of diabetes is now being replaced by the opposite extreme, and deprecates this tendency.

The Treatment of Diabetes with Oatmeal.—MAGNUS-LEVY (*Berlin. klin. Woch.*, 1911, xlviii, 1213) believes that the beneficial effects obtained by the oatmeal diet in diabetes are to be explained mostly by the absence of meat from the diet. He says that the oatmeal cure should always be preceded for a few days by a diet containing a minimum amount of bread—less than 50 grams. The oatmeal diet should continue for a period of three or four days and then be followed by one or two green vegetable days. This process is repeated if necessary, but

the treatment must not be continued for weeks at a time. Magnus-Levy says that this treatment is only necessary for the moderately severe and the severe cases. The method must be followed, but with great care as to details, and daily quantitative determinations of the amount of sugar in the urine are necessary to control the treatment. Magnus-Levy gives the details of the treatment in a case treated by this method. He says that equally good results may be obtained in some individual patients with rye or wheat meal instead of the oatmeal, but believes that oatmeal starch has certain unknown qualities that makes it superior to other starches for the majority of diabetic patients.

A Physiological Investigation of the Treatment in Hemoptysis.—WIGGERS (*Arch. of Int. Med.*, 1911, viii, 17) says that the perusal of recent text-books on internal medicine indicate the chaotic state that the management of pulmonary hemorrhage is in today. Adrenalin, ergot, digitalis, and strophanthus have been recommended by some authorities because of their constricting action upon the pulmonary bloodvessels and the slowing of the heart beat. Others deny their efficacy because of the rise of blood pressure induced by them. Atropine has been advised on the assumption that the dilatation of the skin bloodvessels caused by it draws blood from the pulmonary circulation, while others have condemned it because of its accelerating action on the heart. Aconite, chloral, and chloroform have been frequently recommended, since they reduce the output of the heart and thus tend to relieve the pressure in the pulmonary circuit. The overdepression of both heart and the respirations are the chief reasons for their non-employment by other observers. Amyl nitrite and other nitrites have also been favored on the ground that they lower the pulmonary blood pressure by reducing pressure in the left auricle. They also cause acceleration of the heart that may more than counterbalance this fall in pressure, and for this reason are pronounced useless by others. Wiggers discusses in detail the theoretical basis of the experiments he performed, and gives his conclusions regarding the various remedies that have been more or less empirically recommended. He found that alcohol-free preparations of digitalis cause a rise of arterial pressure and an immediate increase of hemorrhage, owing to the increased output of the right ventricle and the constriction of the pulmonary vessels. They do induce a temporary fall in venous pressure and a reduction of venous hemorrhage lasting as long as the heart remains slowed. This is shortly followed by an increased pressure and hemorrhage when the slowing action is lost. The experiments showed similar effects with strophanthin as those observed with digitalis, except it failed to slow the heart, consequently no beneficial effect of strophanthin upon pulmonary hemorrhage, whether from arteries or venis, can be assumed. Ergotoxin temporarily decreases the pulmonary arterial pressure because of its depressant action on the heart. This is followed by an increased pressure due to a secondary augmentation of the heart. The pressure and hemorrhage from the pulmonary veins are permanently decreased, owing to a persistent constriction of the smaller vessels. The action of ergotoxin on the heart and circulation wanes as the loss of blood continues. Pituitary extract elevates the systemic

arterial pressure by virtue of its peripheral constriction and in spite of a weakening of the left heart. Pituitary extract also causes a fall of pressure throughout the pulmonary circuit because of a decrease in the amplitude of the contractions of the right ventricle. There was no effect upon the expirations except in severe hemorrhages when it sometimes lessened the amplitude of dyspneic respiratory movements. Large doses of chloroform cause a fall of pressure within the pulmonary circuit due to the depression of the heart aided by the diminished respirations. Small doses of chloroform lessen the respiratory movements in hemorrhage and so decrease the pulmonary pressure and hemorrhage without affecting the heart. The nitrites and nitroglycerin cause a general increase in pressure throughout the pulmonary circuit on account of the increased rate and amplitude of the heart, consequently they also cause an increase of the hemorrhage. They may cause a reduction of hemorrhage in the stage when they induce a reduction in the depth of the respiratory movements, which is a symptom of dangerous depression and is accompanied by a weakened systole of the heart. Wiggers concludes by discussing the application of these remedies to cases of pulmonary hemorrhage upon the basis of his experimental work. He says that the chief object of treatment is to promptly reduce the bleeding in the early stage by such drugs as lower the pressure within the pulmonary circuit. He says that this cannot be accomplished by vasomotor drugs such as nitroglycerin or nitrites, and that cardiac depressants, such as chloroform and pituitary extract, must be resorted to. If hemorrhage is continued until the heart is very rapid and the respirations accelerated, deep, and forcible, it is an indication that the heart and bloodvessels no longer react in a typical manner to certain drugs and that the anemia of the cerebral centres is being felt. During this stage it is important that the blood supply of the brain be not reduced by the drugs which check hemoptysis. Hence the drug that combines an ability to elevate systemic arterial pressure and simultaneously to lower that in the pulmonary circuit is the ideal physiological agent to employ during this stage. Wiggers says that, of the drugs investigated, pituitary extract is the only one that possesses his fortunate combination of actions.

Phenylcinchonic Acid in Gout.—Georgiewsky (*Deutsch. med. Woch.*, 1911, xxxvii, 1030) has employed phenylcinchonic acid in the treatment of gout because of its action in markedly increasing the excretion of uric acid in the urine. He says that the majority of patients so treated have shown an improvement in both the subjective and objective symptoms. These results have also been obtained by a number of other observers. The author gives the remedy in doses of 0.5 gram three or four times a day for periods of from five to ten days. No outward effects have been observed from its use.

Indications for the Vaccine Treatment of Disease.—Reiter (*Berl. klin. Woch.*, 1911, xlviii, 1235) says that vaccine therapy should never be resorted to in general infections. Local suppurations of all kinds, including local tuberculous infections, are most suitable for vaccine treatment. An autogenous vaccine gives the best results. Autogenous vaccines are absolutely indicated in infections due to the

colon bacillus. If the case is urgent, polyvalent vaccine should be used until an autogenous vaccine can be prepared. Reiter believes that it is most important to begin with small doses, and local reactions must be avoided. An interval of at least five days should elapse between injections. Furthermore, this interval should be lengthened if the dose of the vaccine injected is increased.

The Serum Treatment of Influenzal Meningitis. — WALLSTEIN (*Jour. Exper. Med.*, 1911, xiv, 73) states that the injection of virulent cultures of Bacillus influenzæ into the subdural space of several species of lower monkeys is followed by the development of an acute inflammation of the meninges, corresponding in chemical, bacteriological, and pathological effects with influenzal cerebrospinal meningitis in human beings. Experimental influenzal meningitis in the monkey is a lethal disease, which terminates fatally in from thirty-six hours to four days after the inoculation. The injected influenza bacilli produce their effects through multiplication, in the course of which they penetrate from the subdural space into the general blood current, from which they may be recovered during life and at autopsy, as is also true of the spontaneous form of influenzal meningitis in man. By repeated injection over a period of many months of living virulent cultures of Bacillus influenzæ into the goat, an immune serum possessing moderate agglutinating and high opsonic power may be produced, which is capable, when injected into the subdural space, of arresting the progress of an experimental influenza meningitis, and of bringing about recovery in monkeys thus affected. As a result of the serum injection, the influenza bacilli in the meninges are more fully englobed by phagocytes, their number is reduced, their capacity of growth diminished, and the eruption into the blood arrested. Along with these effects go, hand in hand, cessation of the local inflammatory process and progressive amelioration of the symptoms of illness, to be followed usually by rapid restoration of health. In view of the highly fatal character of influenzal meningitis in human beings, the employment of an immune serum by subdural injection is recommended. Undoubtedly it will be necessary to apply the serum early and by repeated injections, by means of lumbar puncture, to secure beneficial results. The early application will, in turn be dependent on prompt bacteriological diagnosis, which can be made, as a rule, by the immediate microscopic examination of the cerebrospinal fluid without the employment of cultural methods. When possible, the microscopic diagnosis should be confirmed by cultural tests.

The Administration of Diphtheria Antitoxin by the Mouth. — CUMBERLEGE (*British Med. Jour.*, 1911, cviii, 2637) sums up the points that, according to his experience, indicate that the administration of diphtheria antitoxin by mouth is superior to the usual method of giving it by injection. He says that results are obtained within a few hours and the action of the antitoxin is little slower if any than when it is given by injection. The dose required is also much smaller. Cumberlege has never given more than 4000 units at one time; his usual practice is to give an initial dose of 2000 units and to repeat this dose if necessary. He says that it is often a good plan to give the anti-

toxin in small repeated doses every two or four hours. Another advantage of this method is that there is less risk of sudden heart failure that sometimes results from the struggling of children to escape the needle. No patient treated by Cumberlege with this method has shown any evidence of serum sickness, whereas rashes or joint pains were frequently observed when the antitoxin was given by injection.

The Wheat Flour Treatment of Diabetes.—Blum (*Münch. med. Woch.*, 1911, lviii, 1433) says that when wheat flour is substituted for the oatmeal as given by the von Noorden method, there is no essential difference in the results obtained. The substitution of wheat flour for the oatmeal has many practical advantages, since wheat flour may be given in many different ways, but the methods of administering oatmeal are limited. Blum discusses the theory of the action of oatmeal and wheat meal in diminishing glycosuria. He thinks that the vegetable days serve to relieve the blood of the excess of sugar, and following this the individual's tolerance for starches increases. Another factor of importance is that animal proteid, especially meat, seems in some manner to diminish the power of the body to burn up the carbohydrates. For this reason meat is excluded from the diet when giving an oatmeal or wheat meal cure. Blum says that the milder forms of diabetes respond to this method of treatment more quickly than do the severe forms. It is often unnecessary to precede the meal cure with starvation vegetable days in the mild cases, and in severe cases it may even be dangerous to do so. The vegetable days should always follow the meal days in the severe cases. The mild cases can take large amounts of carbohydrates, usually from 200 to 250 grams, with an equal amount of butter, and in some cases from 50 to 75 grams of vegetable proteid or three or four eggs. He gives moderately severe cases 125 to 150 grams of meal, but allows them as much butter as he does the mild cases. The meal cure is of special value in the treatment of the severe cases with acidosis. In this class of patients care must be used not to give too large quantities of carbohydrates. Blum says that not more than 100 grams should be given at first. After a day or two this amount should be reduced to 50 or 75 grams for a few days, and then the diet should be restricted to green vegetables for a day or two. During the meal days, 125 grams of butter, 50 to 60 grams of vegetable proteid, and the yolks of from four to six eggs are also given. There is no definite rule as to the amount of carbohydrate to be given, but it should be diminished according to the severity of the individual case. Acidosis is much less apt to occur with the meal treatment of severe diabetes, and the glycosuria disappears more rapidly. Blum has treated thirty-five cases with wheat flour in place of oatmeal in the von Noorden diet, and says that the results have been equal if not superior to that obtained with oatmeal.

PEDIATRICS

UNDER THE CHARGE OF

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Further Reports on the Rumpel-Leeds Phenomena in Scarlet Fever.—In relation to recent articles on the Rumple and Leeds sign, it is interesting to note that ALBERT MAYR (*Münch. med. Woch.*, 1911, lviii, 1359) examined 100 cases taken from a skin clinic, in which there was no question of scarlet fever, to determine whether this sign was present in other cases. Twenty cases of this series gave an absolutely positive result. The technique was carefully followed out according to Rumpel and Leeds. Of the 20 positive cases, 14 were females and 6 males. They were of all ages, and there were no pathological skin conditions above or below the area of examination. Scarlet fever was absolutely excluded in every case. The typical hemorrhages around the elbow appeared in from three to ten minutes and lasted from two to four days. Mayr, therefore, holds that the formation of hemorrhages from compression of the upper arm can not be held pathognomonic of scarlet fever, since he has shown that it occurs also in cases with skin and venereal affections, and is especially strong in lupus, syphilis, eczema, psoriasis, and gonorrhea.

Hemorrhage of the Adrenals in the Newborn.—GEORG MAGNUS (*Berlin. klin. Woch.*, 1911, xlviii, 1119) reports a series of 124 infants who died either at or within eight days of birth. In 8 of these cases the necropsy revealed macroscopic hemorrhages in one or both suprarenals. Two of these 8 cases were delivered spontaneously, 3 by version, 2 were foot presentations, and 1 was delivered by Cesarean section. The labors in most of the cases were difficult. Three had asphyxia, and the Schultze method of swinging was employed. In all but 2 cases the infants died within eight hours of birth. The autopsy in these cases showed usually anemia and icterus, and in every case hemorrhage with free bleeding in one or both suprarenals. In some cases the suprarenals were surrounded by a large blood cyst from the hemorrhage. The author quotes a long list of writers who have reported this condition. All are agreed that the destruction of the parenchyma is most marked. The capsule is either unaffected or is secondarily so. The etiology of this condition is doubtful. Among a number of theories may be mentioned fatty degeneration of the adrenals, eclampsia in the mother, trauma during labor, and pressure of the liver on the vena cava. Materna believes in a hyperplasia of the parenchyma causing a disposition toward hemorrhage. It has been found by many observers that abnormal changes, such as congestion and hemorrhage, are almost constant in the adrenals of still-born infants and those dying shortly after birth. Clinically differentiated, one type exhibits progressive symptoms of peritonitis; one type is apoplectiform, with delirium, convulsion, and coma, ending within a few hours or days.

This is the most common form. The presence of icterus is noticed in a large number of the cases reported, but the production of this sign is problematical.

A Rheumatoid Condition of Measles in Infancy.——M. Feibelmann (*Münch. med. Woch.*, 1911, lviii, 1560) reports an acute, polyarticular inflammation occurring a few days after an eruption of measles in a six-months-old infant. The infant showed the typical symptoms and eruption of measles. There were no Koplik spots. The temperature was 39.3° C. Under treatment the eruption faded rapidly. Several days later the infant developed intense swelling and redness of the dorsum of the right foot and joints of the great toe, the dorsum of the left foot, the joints of the right hand, and the right elbow-joint. All the affected joints were intensely tender. Examination of the heart and mucous membranes was negative. The treatment consisted of aspirin internally and local application of aluminum acetate. The following day showed the same involvement of the right hip- and knee-joints. Sweating was not observed and the spleen was not palpable. The axillary and inguinal glands were not enlarged. By the third day the joint conditions began to improve and the temperature was normal. The leukocytoses was 12,000. In four or five days the symptoms had disappeared and the child had entirely recovered. At no time could any cardiac involvement be demonstrated. Feibelmann concludes that there was a direct etiological connection between this polyarticular affection and the measles which developed five days previously; in other words, he considers this an arthritis of measles. Acute articular rheumatism is a rarity in infancy, and some authors deny that it ever occurs in the early months of life. There was no evidence of tuberculosis, syphilis, serum disease, or gonorrhea as a causal factor in the case. The intense inflammatory reaction, the redness, and external tenderness in this case are not seen in a pneumococcus arthritis. Finally, the severe constitutional symptoms of a septic arthritis were entirely absent. Joint complications frequently occur in the various infectious diseases, such as scarlet fever. They are, however, extremely rare in measles, and Fritsch, in a recent search through literature for this particular complication in measles was able to find but 5 authentic cases. Feibelmann mentions 4 additional cases, 2 cases credited to Kompe, 1 to Spitzy, and 1 to Olinto, which, with his own case just described, make a total of 10 cases. In a number of these cases the condition developed finally into joint effusion or chronic arthritis.

Clinical Aspects of Acute Appendicitis in Children.—Harold Collinson (*The Practitioner*, 1911, lxxxvii, 61), in emphasizing the clinical difference between appendicitis in children and in adults, states that it is the commonest and most important surgical disease of the abdomen in childhood. Most of the cases occur between the ages of five and fifteen years. In children the appendix is comparatively larger, lymphoid tissue is more abundant, and there is a shortness and lack of development of the omentum. The causes of appendicitis are similar to those of adults, careless feeding and catarrhal diseases probably taking the lead. The difficulties in making a diagnosis in infant children are great. Pain, a constant symptom, is often ascribed to an

ordinary gastro-intestinal attack. Nausea and vomiting may be absent even in peritonitis. It is hard to determine and estimate abdominal rigidity. A rise of temperature is so common in children that this sign is not absolutely reliable. Fever in appendicitis usually begins some time after the initial pain. A sudden drop is a danger signal, and may mean gangrene or perforation. In gastro-enteritis, vomiting is earlier and precedes the pain. Abdominal pain is less severe and true abdominal rigidity is absent. It is a grave mistake to treat appendicitis with a purgative. The chest should be carefully examined in every sudden onset of illness in children because of the abdominal symptoms occasionally observed. There is no real rigidity in this case. The onset is just as sudden in intestinal obstruction as in appendicitis. Abdominal tenderness and rigidity are usually less marked, distention is earlier, and pyrexia is absent. The condition may occur during an attack of appendicitis from adhesions. A rising pulse rate disproportional to the temperature is a danger signal. Tenderness and rigidity are the most important symptoms we have, although they are often not marked. The prognosis in children is doubtful, and depends on the virulence of the affection and the method of treatment. Apart from early operation the prognosis in children under ten years is bad. Above five years, with early operation the outlook is good, below five years it is not always serious. The indiscriminate use of purgatives is a large factor in the fatal termination of many cases. In the treatment, a careful examination is imperative to establish a diagnosis. Having made a diagnosis of appendicitis, operation or the waiting method may be chosen. The Ochsner method of absolute starvation for four days is not applicable in children. The only safe course is operation, and this should be urged even during the first forty-eight hours because of the inability to predict the subsequent course of the disease, especially as in these patients the symptoms are so misleading and the margin of safety is small. During the second stage of the disease operation should be advised, but as little manipulation as possible should be observed. After the subsidence of a case the appendix should always be removed. The keynote of treatment is operative procedure at the earliest possible moment.

Early Cardiac Paralysis and Hemiplegia in Diphtheria.—Cresswell Burrows (*Brit. Jour. Child. Dis.*, 1911, viii, 311) reports a case of nasal and faucial diphtheria in a girl, aged four and one-half years, in which cardiac involvement appeared on the eighth day. Up to the thirteenth day the cardiac symptoms were distant first sound of the heart, vomiting, and disturbed rhythm of the beats, albuminuria. So far the treatment was adrenalin solution, 1 to 1000, ♏x every four hours. On the thirteenth day cantering rhythm, or *bruit de galop*, developed and vomiting continued. On the seventeenth day the heart was much dilated, pulse very rapid, but the cantering rhythm had disappeared. Tincture of digitalis in doses of 5 minims were now added to each rectal feeding every four hours. The pulse rate was 124. Three days later the pulse rate had dropped to 72, and in three more days the digitalis was discontinued. On the eighteenth day the pulse was still irregular, the heart still enlarged, but the heart sounds stronger. Albumin was still present in the urine. Up to the twenty-second day

the cardiac condition gradually improved, although vomiting still continued at intervals. There was some paresis of the left labial muscles, and nasal voice. Paresis of the sphincter vesicæ developed, and tincture of belladonna, ♏x, and adrenalin, ♏xx, were administered in the nasal feedings. On the twenty-sixth day reduplication of the second sound appeared, and lasted sixteen days. On August 4 external paralytic squint appeared. The knee-jerks were absent on the forty-second day. Three days later paralysis occurred in the left arm, and shortly afterward in the left leg. There was no aphasia. On the seventy-third day, thirty days after the onset of hemiplegia, the arm and leg were almost well. There remained only paralysis in the extensor muscle of the thumb and the peronei of the leg. The child was discharged in this condition. After four months of electricity and massage, the affected muscle had improved but still showed weakness. The knee-jerks were still absent. Very few cases of hemiplegia following diphtheria are recorded. Dr. Rolleston, in searching the whole literature, found only 65 cases. In the present case there were no mental symptoms, although some cases show motor aphasia. Cases of early cardiac paralysis in diphtheria are usually fatal. Among 326 cases of paralysis severe cardiac paralysis occurred in 33 instances. This form occurred in 10.1 per cent. of all forms of paralysis and in 2.4 per cent. of the total diphtheria cases.

The Specific Organism of Scarlet Fever.—A. E. Vipond (*Archives of Pediatrics*, 1911, xxviii, 564) publishes a preliminary report of his investigations in scarlet fever to determine a specific organism. He believes that the enlargement of the lymph nodes in infectious diseases is due to the irritation from the specific organisms of the diseases, the portal of entry being the tonsil. The infection is then carried to the lymphatic system. A number of organisms have been isolated in scarlet fever and claims set up for their specificity. Such are the coccus described by Class, of Chicago, and the streptococcus isolated by Gordon and Klein. Investigators, however, incline to the belief that the streptococci in scarlet fever are secondary invaders and not the specific organisms. Vipond, believing that the specific organism would be found in the lymph nodes, obtained lymph from enlarged glands in 7 cases of scarlet fever. This lymph, under strict antiseptic precautions, was inoculated into slants of Agar, blood serum, and broth. There resulted a raised white growth which turned out to be bacilli. This bacillus, when isolated, proved of rapid growth, and grew rapidly on all different media, including dextrose agar, blood agar, plain agar, blood serum, and broth. In each of the cases cultures of this same bacillus were obtained. Out of the 7 cases Vipond obtained a pure culture of this bacillus in 5 cases, 2 from inguinal nodes, 1 from axillary nodes, and 2 from anterior cervical nodes. Regarding this bacillus as the specific organism, he injected broth culture of it into monkeys, hoping to develop scarlet fever. The monkeys were all healthy and showed no glandular involvement before inoculation. The first monkey inoculated developed general involvement of the glandular system in forty-three hours. It became quite ill, and on the fifth day developed a red rash, a typical strawberry tongue, and died. The same bacillus was recovered from the enlarged glands. The other three monkeys

all showed the following symptoms after inoculation: Enlargement of the lymph nodes in the axillary and inguinal regions; engorgement and congestion of the throat; appearance of a red rash on arms, shoulders, and body; a tongue typical of scarlet fever, malaise, anorexia, and fever; free desquamation continuing as long as three weeks. The same bacillus was recovered from all three cases from lymph taken from an enlarged node. Inoculation of the recovered bacilli into a fifth monkey and two rabbits reproduced the same disease in these animals, with the recovery subsequently of the same bacillus. Koch's law was carried out to its fullest extent in these experiments. The monkeys and rabbits readily developed the disease. The shortest incubation period was two days, and the longest five days. The lymphatic nodes were unusually palpable within thirty-six hours. No suppuration in any instance occurred at the point of inoculation. Streptococci would likely have had this effect. Cultures show this organism to be a long bacillus with rounded ends, staining variably with Gram, and occasionally showing a beaded structure. Some cultures show sluggish oscillatory motility. The organism is an active spore former, the spores being endogenous. On sugar media it produces acid with gas formation. It coagulates milk with formation of acid. Vipond subsequently succeeded in producing scarlet fever in a monkey and in a rabbit by direct contagion from monkeys and rabbits suffering from that disease, and recovered the identical bacillus from their lymph nodes.

OBSTETRICS

UNDER THE CHARGE OF

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Vaccines in Puerperal Sepsis.—Polak (*Bull. Lying-in Hosp. N. Y.* December, 1910) has studied the influence of vaccines on puerperal septic infection. He finds that each case, whether following labor or abortion, must be studied individually, and that the determination to use vaccines will depend upon the evidence present if nature is competent or incompetent to circumscribe or localize the infection. Care must be taken to avoid interference with the genital tract during the acute stage to avoid the spread of the infection. Surgical interference should not be practised so long as the patient's general condition improves. All operations should be postponed until after the acute stage is passed. After the uterus is thoroughly emptied, at the time when infection develops, no further disturbance of the pelvic viscera should be practised. In the subacute stages vaccines may help by increasing the patient's resistance and powers of recovery. If drainage be employed, it should be extraperitoneal, if possible. Thrombophlebitis is considered a conservative process and should not be disturbed.

The Injection of the Serum of Pregnancy in the Toxemia of Gestation.—RÜBSAMEN (*Zentralb. f. Gyn.*, No. 21, 1911) has endeavored to modify acute toxemia of pregnancy by injections of the serum of a pregnant patient. No results followed the treatment.

Tuberculosis in Pregnancy.—SCHAUTA (*Monatss. f. Geb. u. Gyn.*, 1911, Band xxxiii, Heft 3, S. 265) discusses the question as to whether tuberculosis advances more rapidly during pregnancy and what should be done regarding the cases. The majority of clinicians believe that the disease progresses actively in pregnancy, 73 per cent. become worse, and 45 per cent. of tuberculous pregnant women die. Old cases relapse in 68 per cent. The change is most apparent some weeks or months after confinement, although such patients may, apparently, have been better during pregnancy. As regards the treatment of these cases, the German sanatoria find that only one-fourth of those treated after four years time have been able to earn anything at work; probably not 25 per cent. recover. Many sanatoria exclude pregnant cases, because of the unfavorable prognosis. The results of Norwegian observers show a mortality of 50 per cent. in cases treated in sanatoria. Among patients having every care, 29 per cent. grow worse during pregnancy. Children born of such mothers rarely live to be twenty. As regards the induction of labor in the first stage of tuberculosis, it is beneficial in 89 per cent.; in the second stage, in 83 per cent.; and in the third stage, in 25 per cent. Where pregnancy was interrupted in the first month, 91 per cent. improved. It is the duty of the physician then to interrupt pregnancy as early as possible. In addition it seems best to sterilize these patients, as tuberculous women conceive easily, and this had best be done by removing the Fallopian tubes.

The Treatment of Abortion Complicated by Fever.—TRAUGOTT (*Zeit. f. Geb. u. Gyn.*, 1911, Band lxviii, Heft 2) has observed 147 cases of puerperal patients having fever, of whom 58 had labor at term. Of these, 10 died, a mortality of 17.2 per cent. Of the remaining 89, 79 had abortion in the first half of pregnancy, usually from the first to the fifth month. Of these there died 13, 16.4 per cent. To investigate the mortality of these cases further, a study was made by bacteriological examination of the blood and uterine contents. Several groups of bacteria were found in the uterus, growing as saprophytes in the decomposing connective tissue and invading the living tissues. These germs produced simply a bacteriotoxic endometritis. The severity of the clinical symptoms depend upon the quantity of bacteria produced and whether or not the discharge has free exit from the uterus. Amoug these germs were colon and paracolon bacillus, yellow and white, staphylococci which do not produce liquefaction, Proteus vulgaris, sudodiphtheritic bacillus, and other bacilli. These bacteria are capable, either alone or in combination, of producing toxins whose absorption may cause severe symptoms. These bacteria, under favorable circumstances can be recognized in the blood, from which they often disappear without causing metastases. The most favorable time to recognize them is while the patient is having a chill, and they are also found in material removed from the uterus by curetting. When they have been diagnosticated by examination, the treatment consists in emptying

the uterus, and if no other bacilli are present, the patient immediately improves. The temperature falls to nearly normal, leukocytosis is less, chills cease, and the patient makes a speedy recovery. One can determine to empty the uterus or to let it alone in accordance with the germs found in its contents. The emptying of the uterus is done by the finger, and a list of 36 cases is appended, showing uninterrupted recovery. These cases were those in which there could be no doubt concerning the fact that saprophytic mucosis was the condition present in the uterus. When streptococci are present the conditions and history of the case are very different. Fever is present for a longer or shorter time after the emptying of the uterus, metastases develop in the genital organs or in other organs, and in a considerable number a fatal result follows. The recognition of streptococci puts the case in the category of those in which interference should not be practised, as each local disturbance lessens the patient's power of resistance and practically results in a fresh infection. Treatment is carried out practically as follows: If a primary examination shows no indication for emptying the uterus, a bacteriological examination of its contents is made by first disinfecting the external genitals, disinfecting the hands and using rubber gloves, introducing a sterile speculum and exposing the cervix, drawing it down with tenaculum forceps, carefully cleansing the surrounding tissues, and introducing Walthard's pencil into the uterine cavity. This pencil is seized with dressing forceps and the secretion of the uterus removed; twenty-four hours later growth of bacteria can be determined and an idea formed of the character of the bacteria present. Decision is then made to immediately empty the uterus or to wait. If the former course is chosen, the external genitals are thoroughly disinfected, and with the finger covered with a rubber glove, any debris, which easily separates, is removed from the uterus; the uterus is pressed down by the external hand, so that a complete and thorough examination of its interior can be made at the same time. The cavity is then packed with xeroform gauze and the vagina also tamponed with the same material. Intra-uterine injections are avoided, because of the danger of spreading the infection. Particles of retained material will be completely separated by uterine contractions and will come away with the gauze, and the uterus is kept well contracted by the administration of some preparation of ergot. To aid in this a firm vaginal tampon is also used. In cases where the cervix is closed after abortion, the effort is made to secure spontaneous dilatation by the use of the vaginal tampon. If this fails, a laminaria tent is placed in the cervix. Placental forceps and the curette are carefully avoided. In cases of streptococcus infection delay is practised, the patient is given absolute rest and the best possible diet, and if no bad symptoms develop, this form of treatment is pursued without interruption. Examination is made of the blood and uterine contents, and importance is given to the leukocytosis as expressing in some degree the patient's power of resistance. The effort is made to wait until the primary uterine infection has subsided, when the uterus is explored by the gloved finger, debris removed, and the gauze packing used as in the first instance. Instruments are never introduced within the uterine cavity. Should the patient suffer from hemorrhage, the effort is made to control it by tamponing the vagina firmly and giving some prepara-

tion of ergot. This treatment usually secures, within twenty-four hours, the expulsion of any retained portion, and if hemorrhage persists, the tampon is renewed and a strip of xeroform gauze introduced within the cervical canal. This tampon is renewed in accordance with the abundance of the discharge, and is used as often as is necessary. It is the rule to find any retained material spontaneously expelled under this treatment. In cases infected by both the streptococcus and diplostreptococcus and gonorrheal bacteria, the same treatment has proved, in his experience, successful. The question as to whether the same sort of bacteria are found in the vagina and uterus in these cases is one of no practical importance, as there is no difficulty in removing the contents of the uterus if reasonable care be taken by the methods already described. As regards the danger of this manipulation, in several thousand cases no accident has occurred. To contrast these results with those of curetting, in 11 cases of abortion or premature labor in which the lochial discharge contained streptococci, treated with the curette, 5, or 45.5 per cent., died.

The Correction of Unfavorable Presentations in Breech Labor Caused by Impaction of the Arm.—SELLHEIM (*Zeit. f. Geb. u. Gyn.*, 1911, Band lxviii, Heft 2) calls attention to the fact that many of these complications arise from artificial rotation of the child's body, which loosens the arm from its normal position across the chest. The effort should be made to avoid such rotation, so far as possible, and it should be accompanied by gentle massage of the uterus, following down the uterus from above. After expulsion has been secured, spontaneous as much as possible, no interference is necessary; the operator must introduce the hand as high as possible and dislodge the impacted arm under complete anesthesia.

The Source of the Amniotic Liquid.—WOHLGEMUTH and MASSONE (*Archiv f. Gyn.*, 1911, Band xciv, Heft 2) have studied the composition of the amniotic liquid, and find reason to believe that it cannot be regarded as a fetal product only. It cannot also be considered entirely as a transudate from the mother's body. It is, however, derived from the blood of the mother. The experiments of the writers show that a normal substance of high molecular concentration circulating in the mother's blood passes directly into the amniotic liquid, and any variations in concentration of the mother's blood directly have influence upon the specific gravity of the amniotic liquid. These and other considerations demonstrate that the mother's blood is in direct relation with the amniotic liquid. Exactly how close is this relationship we do not as yet know. It is, however, sufficiently ascertained that while the mother's blood does not directly participate in the amniotic liquid, it can transmit substances to this appendage of the fetus.

Glycogen in the Placenta.—FLESCH (*Monatsschrift f. Geburts. u. Gynäk.*, 1911, Band xxxiv, Heft 1) has made investigations to determine the presence of glycogen in the placenta and in the glands of the uterine decidua. He examined 9 placentæ at full term, 1 at seven months, 8 from abortions from six weeks to five months, 1 from tubal pregnancy, and 5 specimens obtained by curetting. He finds that

the placenta at full term contains glycogen, but decidual tissues also contain it, although some cells may be found free from it. The fetal portion of the placenta contains less glycogen than the maternal. The greater number of villi of the chorion, at full term, are free from glycogen, and this substance is found most often in the connective tissue; the syncytium contains it frequently, but in very small quantity. The amnion and chorion are regularly found to contain a small portion. Especially noteworthy is the abundant quantity of glycogen in placentæ before full term. As the Langham's layer of cells disappears, glycogen in the fetal tissues also grows less in quantity. In the placenta at full term the maternal tissues contain by far the greater quantity of glycogen. This substance is also present in the uterine glands and in the uterine epithelia. In normal uterine epithelia glycogen was found in granules in the cells of the uterine glands. These granules surround the nucleus and disappear entirely toward the poles of the cell. In rare cases granules were found at the base of the cells, closely piled upon each other. In the normal mucous membrane the granules usually contain glycogen, and in no case was the mucous membrane of the uterus entirely free from glycogen. The uterine glands, however, differ greatly in the amount which they contain. Where the mucous membrane had been the site of inflammation glycogen was also found, and in greater quantity than in the normal glands. The uterine glands in the membrane of the pregnant uterus were rich in glycogen, although no difference could be detected between the compact and spongy layers. It is interesting to note that the amount of glycogen found in the various cells may be taken as an indication of the activity of the uterine glands, for the increased quantity of pregnancy suggests that this substance is of value in the nourishment of the pregnant woman. This substance is never to be taken as a degenerative product, but is the result of a physiological process. It was formerly supposed that glycogen existed in cells in a dissolved condition. Flesch, however, found this substance in granules of varying size and thickness.

The Technique of Extraperitoneal Cesarean Section.—Sellheim (*Monatssch. f. Geburts. u. Gynäk.*, 1911, Band xxxiv, Heft 1) describes efforts which he has made to simplify the performance of suprasymphyseal section. He has devised an instrument for grasping the fetal head, which he terms a "grasping lever," and which enables him to extract it from the uterus with the least possible disturbance of the uterine wound. He believes the best results are obtained by incising the uterus as low down as possible and in the median line. He believes that during the extraction of the child the abdominal tissues should be carried as far up as possible and held firmly in that position. The instrument consists of a solid handle separating into two blades, joined at the tips by a narrow portion. The blades diverge in a curved fashion and accommodate the average fetal head. The instrument is slipped over the head and the head slowly and cautiously raised out of the uterine cavity.

Serum Therapy in the Toxemia of Pregnancy.—Freund (*Zentralbl. f. Gyn.*, 1911, No. 27) has tried the effect of serum from pregnant animals injected intravenously in doses of 30 to 40 c.c. In 3 cases

of skin lesions occurring in pregnancy, prurigo, urticaria, and erythema, the result was very good, for, two hours after the injection the intense itching, irritation, and disturbance subsided and the patients recovered. The serum was also tried in some cases of eclampsia, in which, after the emptying of the uterus, the kidneys acted sluggishly and the chlorides were especially deficient in excretion. The best results were obtained, however, by prompt delivery, as in 497 cases of eclampsia it was found that those delivered during the first hour after the first convulsion showed no maternal mortality.

Bacteriological Examination of Patients Having Fever during Labor. —Sachs (*Zentralbl. f. Gyn.*, 1911, No. 27) believes that in patients having wounds fever is much more apt to occur, especially in the presence of hemolytic streptococci. As wounds and lacerations of the connective tissue develop, so the danger greatly increases. In these cases one must avoid operative interference, if possible, and choose that form of delivery which is attended by the least laceration and violence.

The Diagnosis and Treatment of Contracted Pelves. — Munro Kerr (*Surgery, Gynecology, and Obstetrics*, July, 1911) contributed a paper upon this subject at the recent meeting of the American Gynecological Society. He relies for comparative measurement of the pelvis and fetal head upon bimanual examination, pressing the head down into the pelvis with the right hand, while two fingers of the left introduced into the vagina note the degree of engagement. With the thumb of this hand the operator feels along the brim of the pelvis and estimates the degree of overlapping of the head. An anesthetic is occasionally necessary, and should the presentation be breech, the method still gives valuable information concerning the size of mother and child. Kerr believes that a careful measurement of the pelvis, both by hand and pelvimeter, should be made in all cases. An attempt should be made to estimate the size of the child's head, and especially the relative size of the head and the pelvis should be studied and made the basis of treatment. This examination should be made at the thirty-sixth week, and again at the beginning of labor, if the pelvic deformity is of moderate degree. In cases of medium deformity, with the true conjugate between 9.3 cm. and 7.5 cm. ($3\frac{3}{4}$ and 3 inches), the size of the conjugata vera is not the important factor in diagnosis, but the relative size of the head and the pelvis, which should alone determine the treatment. In these cases the treatment should be based upon the relative size of the fetal head and the maternal pelvis; if the choice of operation be based only upon the size of the pelvis, mortality and morbidity must result. One who is skilled in the method of examination described can almost always tell whether spontaneous labor may be expected. His experience in cases where the true conjugate was less than $3\frac{3}{4}$ inches, and where the forceps were applied, was so unsatisfactory that he now selects cases with great care, not applying the forceps until engagement and moulding have distinctly developed. In 130 cases with the true conjugate varying from 7.5 cm. to 8.7 cm., delivered by forceps at the earliest possible moment, the fetal mortality ranged from 15 to 46 per cent. In 22 cases of similar pelves, in which spontaneous delivery was procured in all possible conditions, the fetal mortality did not exceed 4.5 per cent.

Kerr would not entirely condemn the use of forceps at the pelvic brim, but believes that forceps should be used where the disproportion between the head and the pelvis is such that spontaneous delivery might have been reasonably expected, and the second stage of labor allowed to go on until there are very definite indications for hastening labor. When forceps are applied the head must be fixed, and the operator must expect to deliver with only moderate traction. No child should die or be seriously injured as the result of forceps delivery. In uncomplicated cases in which these accidents occur, the judgment of the operator has been at fault. Kerr, in recent years, has not performed Cesarean section late in labor, in cases that had been under his care through the entire time of parturition, and in which he had determined that spontaneous birth or forceps was possible. Craniotomy he has performed seventeen times in recent years, but in no case seen early in labor and under his care in the first stages of labor. Pubiotomy, he considers a reserve operation, which has a very limited field after spontaneous labor has failed to deliver, and one trial with forceps, with the patient in Walcher's position, if the pelvis be flat, has been made. His belief is that we have now reached the point in the practice of an obstetric surgeon where the number of pubiotomies will be in inverse ratio to a surgeon's diagnostic skill and judgment. Kerr's results in induced labor in hospital practice have not been satisfactory, for the early and late mortality with the children is slightly over 30 per cent. In domestic practice the results have been uniformly good. In selecting cases for this treatment he would choose those in which the true conjugate was not less than 8.1 cm., the pregnancy must have advanced at least to the thirty-sixth week, and the patient must be in her second or subsequent pregnancy, the first pregnancy ending in a test labor and showing liability to complications. In the thirty-sixth week the patient is examined under anesthesia and the relative size of the head and pelvis determined. If the head can be made to engage at the pelvic brim, labor should be induced. Craniotomy, Kerr thinks, cannot be limited strictly to cases where the child is already dead, but may be applied to cases in which the child has been injured or subjected to birth pressure to such a degree that its life has been seriously threatened. In cases suspected of infection, craniotomy has a mortality of about 8 per cent. In cases of dead or dying children it is the only treatment to be considered, when the pelvis is not highly deformed. In young healthy patients who are probably infected and the child already injured by birth pressure or efforts at delivery, craniotomy is probably the safest operation, where the pelvis is not highly contracted. If Cesarean section be chosen in infected cases, panhysterectomy is the preferable operation. Extraperitoneal section affords but one possible advantage over the classic section, that the cicatrix of a carefully stitched wound in the lower uterine segment may be firmer than one in the active contractile body of the uterus. In order to escape infection in suspected cases during Cesarean section, Kerr suggests that the placenta and membranes be pushed down into the vagina and not pulled up and delivered through the uterine wound. He is accustomed to very carefully wash out the vagina, cervix, and the child's head with liquid soap and normal salt solution. During Cesarean section the patient is placed on the operating table with her pelvis

slightly lower than her head. The skin is cleansed by iodine; the abdomen and uterus are opened in the usual manner; the abdomen carefully protected by gauze; the child is extracted by the feet. The operator now puts on a fresh pair of gloves, separates the placenta completely and covers it over with gauze, and then pushes gauze and placenta down through the cervix into the vagina. Several pieces of gauze are then pushed through the cervix above the placenta and removed from the vagina by an assistant.

Anteflexion of the Cervix and Spasm of the Uterine Ligaments in Relation to Retroversion, Dysmenorrhea, and Sterility.—Reynolds (*Surgery, Gynecology, and Obstetrics*, July, 1911) has treated cases of anteflexion of the cervix by preliminary dilatation and curetting and then measuring the length of the cervix and the external os to the point of flexion. The posterior lip of the cervix is divided by scissors in the median line up to this point. The angle between the line of the cut and the edge of the external os on each side is then sutured into the extreme end of the upper cut, after the manner of Dudley's method of discission of the cervix; two sutures, one on each side, are introduced. The anterior lip of the cervix is then seized by the volsellum and drawn strongly backward, putting the anterior wall sharply on the stretch. The vaginal wall is then divided transversely with the knife, just in front of the cervix, the cut being usually just wide enough to admit a finger and carried completely through the vaginal wall with the knife and scissors exposing the bladder. The finger is then passed into this cut and the bladder freed from the vagina and cervix well up toward the anterior surface of the uterus. A similar blunt dissection separates the anterior attachments of the vault of the vagina and the base of the bladder, well out to each side. It is important that this separation should be carried above the angle of the flexion. The edges of the vaginal wound are closed by transverse sutures, including nothing but the vaginal walls, thus lengthening the anterior vaginal wall. Profuse bleeding may be observed from the vaginal wall, but if blunt dissection be employed there is no other hemorrhage. In cases where careful examination has led to the belief that sterility is dependent on partial retention of secretions in the cavity of an anteflexed uterus, the operation has been very successful.

GYNECOLOGY

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Ovarian Causation of Uterine Myomata.—Seitz (*Münch. med. Woch.*, 1911, lviii, 1281) calls attention to the fact that the growth of the uterus is certainly influenced by the ovaries, since, when these are

removed the uterus atrophies. That this is not due to nervous influences is shown by the fact that if the ovaries are removed and a portion of one replanted in some part of the body, so that all nervous connections are severed, uterine atrophy does not occur. The author believes that the development of myomata is also dependent upon the internal secretion of the ovary, since no case is known of the development of myomata before puberty nor after the menopause. This relationship is also indicated by the reduction in size of myomata which takes place after castration, and after the destruction of ovarian activity by means of the *x*-rays. It seems probable, therefore, that the origin of myomata is due to the presence of some altered ovarian secretion.

Sea Bathing in Gynecological Affections.—Prof. Bossi (*Gaz. d. Ospedali e d. Cliniche*, 1911, xxxii, 707) makes a strong plea for what he terms "thalassotherapy" in the treatment of many conditions, sufferers from which are ordinarily subjected to serious and mutilating surgical operations, entirely too many of which he believes are being performed at the present day. He considers it the duty of teachers and heads of large clinics to advocate in many cases a return instead to the thermal and medicinal therapeusis of a generation ago, laying especial stress on the advantages of sea bathing in practically all chronic gynecological affections. In order to be effectual, however, this must be carried out under suitable conditions, which are: An equable mild climate with plenty of sunshine, warm water, and a smooth sea, conditions which, in Europe at least, are to be found only along the Mediterranean and Adriatic Seas and a very small portion of the Atlantic Ocean. The chief advantages obtained from sea bathing are due, according to Bossi, to breathing the sea air, to the actual immersion of the body in sea water, the duration of this being graduated from fifteen minutes at the beginning of treatment to two or even three hours, and to the exposure of the body to the sun which necessarily accompanies the bath. In a few specially selected cases swimming, rowing, surf bathing, and hot sea-water baths should be ordered in addition. By this method of treatment Bossi believes, as a result of many years' experience as director of a large gynecological clinic in a Mediterranean coast city, that great improvement may be obtained in many cases of the following gynecological affections: Chronic pelvic cellulitis and parametritis, chronic adnexal inflammations hyperplastic cervicometritis, puerperal subinvolution, residual hematocele, prolapsus uteri, versions and flexions, even when accompanied with adhesions, chronic endometritis, and fibromyomata. He emphasizes the fact, however, that the treatment should always be directed by a physician in accordance with the needs of the individual patient, and the local conditions prevailing at the resort at which the cure is being taken.

After-results of Appendectomy.—König (*Med. Klinik*, 1911, vii, 875) believes that in most cases persistent trouble after appendectomy or other abdominal operations is due to the formation of adhesions. He believes that certain individuals have a much greater tendency to the formation of adhesions than others, but that in any case where even the finest adhesions are once formed, any operation

may increase them. Since adhesions may form during any attack of appendicitis, the only sure way to avoid them is to remove the appendix before they have time to form; in other words, as soon as the diagnosis is made. It should be our rule to treat appendicitis as we do strangulated hernia—operate at once, do not wait for the interval. König believes that packing off the peritoneum with gauze should be avoided as much as possible, as it favors the subsequent formation of adhesions; he does not do it even in cases where the appendix is gangrenous, if no perforation is present. He lays great stress on the importance of the postoperative treatment in the prevention of adhesions. An intestine that is in motion does not form adhesions as quickly as one that is quiet, therefore he starts in on the day of operation with hot air treatments to stimulate peristalsis. A daily passage is secured by the use of glycerin enemata. The patients are encouraged to move their legs early, and are gotten out of bed as soon as possible, often on the second day after operation. In cases where adhesions already exist at the time of operation he recommends giving two tablespoonfuls of olive oil by mouth and an oil enema of 250 c.c. daily. At the end of the first week systematic abdominal massage should be begun, at first avoiding the field of operation, later, however, including the whole abdomen. He has these patients change their position in bed frequently, and assume the knee-chest posture from time to time. Very beneficial lasting results have proved the value of these methods of treatment in König's practice.

Relation Between Corpus Luteum and Breast.—Bouin and Ancel (*Presse Méd.*, 1911, No. 55, p. 577) believe that in studying the phenomenon of lactation two distinct phases must be kept in mind—(*a*) the morphological development of the glandular tissue of the breast; (*b*) the occurrence of secretory activity—these two phases being dependent upon totally separate causes. Since it has been proved by nerve sections and by transplantations that nervous reflexes cannot be considered as inciting the mammary gland to activity, we must have recourse to the theory of a chemical reflex—a hormone, developed in some distant organ, and acting on the mammary gland. In order to discover the source of this hormone, which Bouin and Ancel suspected to lie in the corpus luteum, they conducted a series of experiments on rabbits, an animal in which ovulation, and consequently corpus luteum formation, does not take place spontaneously, but occurs normally only after coitus; it may also be brought about artificially by rupturing perfectly ripe Graafian follicles with a needle or fine scissors. In this way, or by allowing coitus with male animals rendered sterile by the ligation of the vas deferens, Bouin and Ancel were able to produce in female rabbits corpora lutea without the development of pregnancy, or of any other condition which might have influenced the results. They found that following such a procedure a tremendous development of mammary gland tissue invariably took place, the acini increasing greatly in number, volume, and complexity. By about the sixteenth day this development had reached its greatest height, and from then on atrophy set in, the acini diminishing in volume, their lumina becoming obliterated, the epithelium desquamating, the ramifications growing less, and the vascularity diminishing. After a normal coitus,

followed by fecundation, on the other hand, the mammary gland continues to develop; the increase in size in the latter half of pregnancy is due, however, not to a further multiplication of cells, but to an accumulation of secretory products in the lumen of the acini; in other words, tissue growth has given place to secretory activity. It was found that in a few cases where coitus did not produce a rupture of follicles, or if all corpora lutea were destroyed by the thermocautery soon after coitus, no development of mammary tissue took place; if the destruction of the corpora lutea is done a few days later, the mammary development which has begun is at once arrested, and atrophy sets in. Bouin and Ancel believe, therefore, that the corpus luteum is the factor in producing the anatomical development of the mammary gland during pregnancy. This theory also explains the recurrent increase in size of the human breast coincident with each menstrual period, this being dependent upon the short-lived "corpus luteum menstruationis" which arises in woman as the result of *spontaneous* follicle rupture. Bouin and Ancel believe that the corpus luteum has, on the other hand, nothing to do with causing the fully developed mammary gland to begin secretory activity, but that this process is dependent upon a second hormone arising from a gland of internal secretion which they have discovered in the myometrium of the pregnant rabbit, and which they call the "myometrial gland."

Treatment of Leucorrhea.—STOCKER (*Gynæcologia Helvetica*, 1911, xi, 160) calls attention to the fact that in every leucorrheic discharge are found many polymorphonuclear leukocytes. These contain a ferment having an albumin-digesting (proteolytic) action, which causes extensive liquefaction of tissue, this expressing itself as purulent secretion. It has been found that there exists in the blood serum an antiferment which fixes this proteolytic ferment. By injection of this antiferment, therefore, purulent processes can be shortened or stopped. It is necessary that the antiferment come into immediate contact with the ferment, as the action is a direct neutralization. Since 1909 Stocker has treated all cases of fluor albus on this principle, with very gratifying results. He uses "leucofermantin" (Merck), introducing a gauze strip soaked in this substance into the cervix after thorough cleansing of the latter. The gauze is changed the next day. If the uterus is much enlarged, showing that the corpus is also affected, 1 to 2 c.c. of the fluid are injected by means of a Braun's syringe under very gentle pressure into the uterine cavity. No douches are given during the treatment, in order better to control results. Of 70 patients thus treated Stocker reports 68 per cent. as being entirely cured of the discharge and the others greatly relieved.

Nasal Treatment of Dysmenorrhea.—BRETTAUER (*Am. Jour. Obst.*, 1911, lxiv, 215) makes a plea for the serious consideration of the nasal treatment of cases of dysmenorrhea in which no gynecological condition can be found to be responsible. In these cases the pain usually disappears within a few minutes after the application of a 20 per cent. cocaine solution to certain areas in the nasal mucous membrane which are composed of erectile tissue, and which always become swollen, hyperemic and hyperesthetic, during each menstrual period. Where the

pain is due to some uterine displacement, inflammation, or other local condition, application of cocaine to the nasal areas referred to above has no effect whatever. In those cases where it is followed by relief of pain, however, Stocker claims that a permanent cure may often be affected by cauterization or other suitable rhinological treatment, and reports four cases of severe dysmenorrhea in unmarried women who were cured by cauterization of edematous nasal mucosa, removal of spurs, enlarged turbinates, etc.

Origin and Dissemination of Renal Tuberculosis.—As the result of a series of experiments on dogs and goats, in which suspensions in sterile oil of tubercle bacilli of varying degrees of virulency were injected directly into one renal artery, PELS-LEUSDEN (*Arch. f. klin. Chir.*, 1911, xcv, 245) believes that the theory that most cases of chronic unilateral renal tuberculosis are of hematogenic origin is correct, the infection occurring probably by means of small tissue particles, fat droplets, or other forms of emboli containing tubercle bacilli, which have passed through the lung capillaries. He believes that isolated tubercle bacilli circulating in the blood may pass through the kidney without doing any harm. In cases of severe caseous tuberculosis of the renal pelvis, with occlusion of the collecting tubules, the process may extend retrograde throughout the kidney by way of the uriniferous tubules. That tuberculosis of the kidneys can arise by retrograde transmission through the lymphatics from the lungs, pleura, or bronchial lymph glands he considers by no means demonstrated. He believes that trauma considered in its broadest sense—as an impairment of any sort of the normal integrity of the tissues—plays a certain role in the development of a local tuberculous focus, but that trauma in the sense of a direct contusion at a given point is not necessary to the development of tuberculosis at that point. As a result, however, of such a trauma, tissue particles and bacilli may be thrown off into the blood stream and then give rise to a chronic tuberculosis at some distant point.

Use of Pituiterin in Gynecology.—In cases of endometritis, metritis, and of menorrhagia due to myomata, ovarian cysts, or inflammatory conditions of the adnexa, BAB (*Münch. med. Woch.*, 1911, lviii, 1554) has seen pituiterin (hypophysis extract) produce marked results in stopping hemorrhage when hydrastis, ergot, stypticin, etc., had been used without result. He injects subcutaneously 2 to 3 c.c. once, or, if necessary, on several successive days, and has had no unpleasant after-effects except occasionally slight labor-like uterine pains. He reports that in 30 cases so treated, in many of which the bleeding had been protracted and profuse, the bleeding stopped on the first day in 33 per cent., on the second day in 36 per cent., and in only 6 per cent. was no effect whatever produced. KLOTZ (*Münch. med. Woch.*, 1911, lviii, 1119) reports equally favorable results from the use of the same substance in the treatment of atonic uterine hemorrhage post partum. He uses for this purpose 0.2 gm. of the gland (represented by 1 c.c. of the preparation made by Borroughs, Wellcome & Co., and by 2 c.c. of that put out by Parke, Davis & Co.), but says that the maximum dose that can be borne is unknown. He considers intramuscular injection to be the proper method of application.

DERMATOLOGY

UNDER THE CHARGE OF

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Pathology of Malignant Epithelial Growths of the Skin.—JOHN A. FORDYCE (*Jour. Amer. Med. Assoc.*, 1910, lv, No. 19, 1624) believes from his numerous investigations that no one agent is concerned in the malignant proliferation of epithelial tumors, and that a multiple etiology is responsible for the cutaneous carcinomata. A strong argument against the theory of the parasitic nature of the disease is the development of epitheliomata following exposure to sunlight, Röntgen rays, and other radiant energy. The action of such chemical substances as arsenic, tar, tobacco, and scarlet-red on epithelium, for which they have a special predilection, goes to show that a variety of agents have the power to stimulate epithelial mitosis which may pass into malignancy. Carcinomata which develop on scar tissue or antecedent conditions of the skin like lupus, syphilis, etc., suggest the idea of misplaced cells in some cases and in others with degenerative processes which interfere with the functional life of the cells, followed as a consequence by overgrowth of the cells.

The Tineas.—R. SABOURAND, an authority, enters upon the subject of the cryptogamic disease at great length (*Brit. Jour. of Derm.*, October, 1910, pp. 334, 335), the following points being of practical interest. It is stated that different forms of fungi are responsible for ringworm and favus, and that in Paris, out of 500 cases, 150 were due to microsporon, 218 to trichophyton, and 52 to favus. Eleven species of microsporon are described by the author, 15 of Trichophyton endothrix, 15 of Trichophyton ectothrix, and 5 of favus, which affect man and certain of the lower animals. No accidents effecting the brain from the use of *x*-rays are recorded. An important practical question discussed is the danger of producing permanent loss of hair from the use of *x*-rays in the treatment of the tineas of the scalp. Sabourand takes the view that if such an accident did occur it was due to an overdose, the same region being exposed to more than one full dose at too short an interval, or to the regulation distance of 15 cm. between the anticathode and the scalp not being adhered to.

(The profession is greatly indebted to Sabourand for our present knowledge of the treatment of the tineas by *x*-rays, his labors in Paris over many years having resulted in much good for therapy.—L. A. D.)

Etiology of Elephantiasis.—G. C. SHATTUCK (*Boston Med. and Surg. Jour.*, clxiii, No. 19, p. 718) directs attention to the relation between edema, hyperplasia of connective tissue, and lymphatic dilatation.

The essential characteristics of the acquired form of the disease are lymphangiectasis, hyperplasia of connective tissue, and chronic edema, and these conditions may frequently be attributed to the interaction of stasis and inflammation, stases always occurring early, and persisting. Inflammation may precede or follow stasis, or may be absent at any stage of the disease, and may be acute or chronic and generally may be traced to bacterial infection. Chronic stasis or inflammation may predispose to elephantiasis, but the disease does not always result even when they occur together. Filaria is an important factor in the production of endemic elephantiasis of some countries, but is not essential to the occurrence of the endemic variety. The disease in regions where filaria abound results indirectly from filariasis through bacterial infection.

Solid Carbon Dioxide in Dermatology.—E. R. MORTON (*Lancet*, August 20, 1910, p. 558) relates his experience in a large number of cases, including capillary and cavernous nevi, port-wine marks, lupus vulgaris, moles, and warts. Of capillary nevi, 212 cases were completely cured by a single application, lasting on the average forty seconds. Other cases had more applications. In cavernous nevi the results were not so successful, although 33 cases were cured by a single application, and 5 incompletely cured or not benefited. In port-wine mark every portion of the lesion had to be treated two or three times. In lupus vulgaris crusts are to be removed and firm pressure made with the crayon for at least forty seconds. The healing process occupied from two to three weeks. The results were regarded as satisfactory. In moles and warts the treatment is eminently successful. In pigmented and hairy moles from thirty to forty seconds are usually required, but the author is not sure as to the permanence of the destruction or loss of the hair due to the freezing. (But little is said about the pain following the application, which some operators find an objectionable feature of the treatment.)

Therapeutic Use of Refrigeration with Solid Carbon Dioxide.—W. A. PUSEY (*Jour. Cutaneous Diseases*, July, 1910) contributes a paper of great interest in connection with this chemical agent which of late has become so popular with dermatologists for the treatment of various affections of the skin. In treating lesions up to the size of one-half inch in diameter, where the lesion is uniform in surface, one application of a mass of the snow, which is moulded or pared as nearly as possible to the size and shape of the lesion, is made. For lesions above an inch in diameter the best practice is to shape the end of the stick of CO_2 into a rectangular form in order to get perfect coaptation of the area treated. Even pressure should be exerted, in order to avoid irregularities in the freezing of the tissues. Warm or cold bathing of the part after freezing relieves the pain. As a rule, no after treatment is called for, beyond ordinary antiseptic precautions. Blebs that form may be emptied or allowed to rupture without surgical interference. Untoward effects seldom result. Scars, if these result, are usually of a benign or excellent character. The list of diseases in which this agent may be employed with the expectation of satis-

factory results is large, among which may be specially mentioned vascular nevus, especially small lesions up to the size of a coin; obstinate chronic inflammatory lesions, as lichen and thickened eczematous patches; lupus erythematosus; senile pigmentary spots of the hands and face; warts and callosities; moles and pigmentary nevi, especially small nevi. For the ordinary forms of cutaneous carcinoma the author prefers other methods of treatment. (The paper is an interesting and valuable contribution to cutaneous therapeusis.—L. A. D.)

Our Knowledge of Pigment Production.—J. E. R. McDonagh (*Brit. Jour. of Derm.*, October, 1910) gives a summary of the discoveries made since the observations of Koelliker in 1860, who found in the epidermis of a fish pigment cells which sent their processes into the corium. Many of these branched cells being found in the corium, he concluded that they originated in the corium. Kebert after him regarded these "chromatophores" (as Koelliker called them) as connective tissue cells which had the power of manufacturing pigment for the supply of the epidermis. Riehl (in 1884) called these pigment cells "wander cells," and because he found them mostly arranged around the bloodvessels of the corium, presumed they built up or derived their pigment from the blood and carried it to the epidermis. Ehrmann in part confirmed Riehl's studies, but stated that the wander cells stop short when they reach the epidermis, the further progress of the pigment being performed by an intermediary cell branched and ameboid in character, and epithelial. Karg transplanted by grafts negro's skin on white skin, and vice versa. The former became white and the latter black, showing that the cells in the corium were the cause of the pigmentation. Ritterer (in 1887) and others since have shown that epidermic pigment had an autochthonous origin. Meirowsky's important recent experiments with the Finsen rays show that pigment was found in the epidermis only, and the origin of pigment is autochthonous. Hemoglobin plays some part in the production of pigment, but is not the source of all. It is impossible to determine the relation blood bears to pigment. It would seem that the production of pigment may be regarded as a metabolic process, affecting the proteid molecule of the cell, this metabolic change being due to the action of a ferment; the studies by several observers in recent years favoring the part played by a ferment, especially that named by Bourquelot "tyrosinase." The further connection between pigment and metabolism is shown in ochronosis, where the cartilage of the body becomes black.

X-ray Therapeutics in Dermatology.—The following is condensed from a lengthy review of a book (just published) by Frank Schultz, by "J. B. L.," in the *British Journal of Dermatology*, for October, 1910. Dr. Schultz is chief of the Light Department at the Berlin Kgl. University Polyclinic, the work being based on an experience with 25,000 *x*-ray applications. It is stated that the two extreme results of the action of *x*-rays are surprising cures and serious injury. The exclusion of unsuitable cases and avoiding all injurious after effects in cases treated is the duty of every *x*-ray therapeutist. The question of idiosyncrasy, or undue capacity of reaction to *x*-rays, is

of great importance from a forensic as well as a therapeutic standpoint. Cases of general reaction are recorded in literature, and also eruptions resembling toxic erythemata (with or without fever), following the treatment of circumscribed, as well as more extended, areas, by *x*-rays. Holzknecht believes that toxic erythemata only follows burns, and are due to absorption of *x*-rays necrosed products. They cannot, therefore, be regarded as cases of idiosyncrasy, and apart from such burns Schultz met with no such reaction in his large experience. Hypersensibility to *x*-rays may vary in the same patient at different times, and hence from a legal standpoint the general question of idiosyncrasy is not so important as the question of the exact dosage employed in a given case. At the Radio-therapeutic Institute, in Berlin, every dose is entered in a record book, and is only administered in the presence of a physician, though it is doubtful if the physician must necessarily be present in the apartment during the entire period of the *x*-ray application, if he personally sees that the current is stopped at the right time. Schultz has not found much benefit from *x*-rays in acne rosacea. He does not employ it in tinea kerion. In sycosis vulgaris good results often follow $\frac{1}{3}$ dose, and cases rebellious to this treatment often improve under combined *x*-ray and high-frequency (unipolar) applications. The treatment of hypertrichosis by *x*-rays was not found satisfactory, inasmuch as, if carried far enough to cure the local growth, atrophic changes in the skin and other grave dangers occur. Hyperidrosis seems benefited in some cases, especially under full doses, but other cases show no improvement, and it is difficult or impossible to determine beforehand which type of case clinically is likely to be benefited. Schultz thinks that the damage to growing bones has obtained undue prominence from the experiments upon animals, for he has not met with such cases.

Neuralgia Paresthetica.—S. SHERWELL (*Jour of Cutaneous Diseases*, June, 1910), gives his experience with a case of this disease, which was fully described in 1906, by Dr. J. C. White, of Boston. The region affected, as, for example, a limb, becomes the seat of a variety of perverted sensations, such as tingling, tenseness, or still more acute superficial tearing, darting pain, with numbing of sensation. It may begin with a glowing sensation, or like the beginning of herpes zoster, and in the author's belief the pains are caused by the same mechanical means, namely, pressure on a nerve and its continuity; but it is a disease of sensory disturbance only, at least in his cases, though Dr. White found some objective symptoms. He concludes that the condition arises from a constriction or pinching of a nerve as it passes through tough fascia, irritation resulting therefrom. Rest and massage produce temporary relief, though not a cure. (In which case the use of heat and cold or friction or massage produced no relief whatever.)

Sporotrichosis in Man.—From the pen of the late and distinguished JAMES NEVINS HYDE, of Chicago, conjointly with D. J. DAVIS (*Journal of Cutaneous Diseases*, July, 1910), comes a valuable article on this comparatively new and but little known disease affecting both man and some of the lower animals, notably the horse ("mycotic lymphangitis in horses"). Experiments upon animals and bacteriological

studies are given and pictured, rendering the lengthy article a valued contribution to medicine. A synopsis of the conclusions of the authors may be given. The type of the dozen or more instances of sporotrichosis in man observed in America practically corresponds with that observed in France and elsewhere in Europe, the disease being due to the organism first described by Schenck, and properly named by Hektoen the Sporotrichium Schenkii. Some of the American cases of mycotic lymphangitis, or epizoötic lymphangitis, in horses are due to the presence of this growth, and should be described as instances of sporotrichosis.

Effect of Radium on the Skin.—Guyot (*Journal of Cutaneous Diseases*, May, 1910, p. 269) gives a lengthy article, with experiments on the subject, in *Archiv. f. Derm. u. Syph.*, 1909, from which the following practical points may be abstracted. In the first two weeks desquamation appears, and in the third week loss of epidermis and hair, followed by ulceration or progressive atrophy of the skin. In the corium there is cellular proliferation and hyperplasia of connective tissue, but the hair papillæ, elastic tissue, and muscles remain unaffected. The blood and lymph vessels are dilated, but no change occurs in their walls. It may be said that radium acts as a physical and chemical irritant, different effects following different periods of exposure, and that reparative changes are slow.

The Skin Atrophies.—Finger (*Brit. Jour. of Derm.*, June, 1910, p. 202) divides all atrophies of the skin into two groups: (1) Firm atrophy, as observed in the last stages of lupus erythematosus and scleroderma, this being found to be reduced in size, thinned, fixed firmly to the underlying strictures, stretched, smooth, shiny, and only with difficulty raised into folds. This is seen especially in scleroderma. (2) In other cases the skin is loose. In cross-section it is also much reduced in size, but is not adherent to the underlying strictures, lying loose, consequently in wrinkles, therefore easily raised and thrown into folds. The latter group include cases like the well-known and depicted one of Buckwald. Pick's "erythromelia" and Neumann's "erythema paralyticum" are undoubtedly commencing stages of idiopathic atrophy, and Herxheimer and Hartmann's cases of "acrodermatitis chronica atrophicans." Finger then goes on to describe other described and recognized clinical forms of atrophy. (There exist a number of beautifully executed wax models of various forms of atrophy of the skin which the abstractor has recently viewed in Professor Finger's museum.—L. A. D.)

Molluscum Contagiosum.—Norman Walker (*Brit. Jour. of Derm.*, September, 1910) enters into the question of the distribution of this disease of the skin, his experience and studies not being in accord with those of Graham Little, who believed there was a connection between the disease and seaports. Walker is much more inclined to the view that public baths are a means of its spread, and refers to the experience of physicians in Damascus, where it was known locally by an Arabic name which meant "the itch of the bath." The field of Dr. Walker's observation was Edinburgh, where the disease seems

to be frequent, 45 cases having been observed in two and one-half years. (In Philadelphia the disease, beyond an occasion of epidemic in a children's asylum, is not only rare, but ill-developed as to the individual lesions, most of them being small and imperfectly formed. —L. A. D.)

Dermatitis Exfoliativa Treated with Quinine.—W. H. Mook (*Journal of Cutaneous Diseases*, September, 1910) directs attention to the value of quinine in full doses in this well-known, but uncommon, disease. A case is reported in which it succeeded in effecting a cure on two occasions, five-grain capsules of the hydrochlorate (preferred to the sulphate), four or five times daily, being prescribed. The author had previously reported 6 cases successfully treated by the same method. No local treatment was used. (It is questionable if cases, such as the one here reported, should not rather be diagnosticated and designated as pityriasis rubra than dermatitis exfoliativa. But irrespective of this point, the therapeutic note given is distinctly valuable.—L. A. D.)

Eucarin, a New Emollient.—G. H. Jackson (*Journal of Cutaneous Diseases*, June, 1910, p. 294) reports favorably of this new medicament emanating from Dr. Unna, of Hamburg. It is made of vaseline, acted upon by a substance obtained from wool-fat, which it is claimed takes up a large amount of water, and is in consequence a very cooling ointment. Unna found it useful in ichthyosis, and Jackson, excellent for various forms of cutaneous disease in which the skin was dry. Thus it is useful in chapped hands and similar conditions of the skin. He usually combined it with cold cream ointment, about ℥iij to ℥j, which proportions make a desirable ointment. It is useful upon the scalp in cases where a distinctly greasy application is not desired. It does not become rancid.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Cultivation of the Leprosy Bacillus.—Clegg (*Philippine Journal of Science*, 1909, iv, 77 to 79, 403 to 415) based this work upon the assumption that the leprosy bacillus derives its nutrition from the products of the tissue cells and the cells of the lesions in which it is encountered. Since this bacillus occurs so frequently within the protoplasm of these cells, a unicellular organism was selected which could be cultivated and which corresponded in a degree to the living tissue cells; that is, an organism which contained both nucleus and protoplasm. The amœba is readily grown upon artificial culture media and further

fulfils the other requirements. The method for obtaining cultures of the leprosy bacillus was essentially as follows: The amœba were isolated from water by adding 1 c.c. of alkaline bouillon to every 100 c.c. of the water in question. After twenty-four to forty-eight hours the surface was examined and if the amœbæ were present a loopful of the surface water containing the amœbæ was transferred to the surface of agar in a Petri dish which had been previously inoculated with cholera vibrios. The amœba-cholera culture was then transferred to the surface of agar slants and after twenty-four hours inoculated with the suspension of leprosy material. These slants were incubated for seven days at body temperature, and the growth transferred weekly to fresh slants. At the end of from four to six weeks, acid-fast organisms were obtained in pure culture by heating the "pure-mixed" culture of the cholera amœba-leprosy to 60° C. for 30 minutes. The acid-fast organisms survived this heating, while the amœba and cholera vibrios were killed. These acid-fast organisms grew readily when transplanted to plain agar and other media. The organisms stained in a characteristic manner by the Ziehl-Nielson method. In order to prove that these organisms were not tubercle bacilli, considerable amounts of the pure culture were inoculated subcutaneously into guinea-pigs. A week later an indurated nodular thickening appeared at the site of inoculation in some of the guinea-pigs. In four weeks the lesions spread over the abdominal walls, the hair over the lesions fell out, the animals became emaciated, and death occurred between four and five weeks after inoculation. Cultures from these guinea-pigs were negative. The smears showed large numbers of acid-fast bacilli, the majority of which were intracellular. Three more guinea-pigs were inoculated in a similar manner and with similar results. The organisms were found not to be tubercle bacilli. In one set of experiments the organisms were carried from pig to pig for three successive transfers. In only one instance was it possible, however, to reclaim the acid-fast organism by growing it in symbiosis with the amœba-cholera culture. Several monkeys were inoculated, all of which proved refractory. The guinea-pigs which were inoculated subcutaneously with a pure culture of the acid-fast organism developed lesions in some instances at the site of inoculation, which bore a certain resemblance to the leprous lesions of man both macroscopically and microscopically. The organisms were short, plump, acid-fast bacilli, occurring mostly in clumps. They grew readily, although slowly, in media which was 1 per cent. alkaline in phenolphthalein. It was noticed that repeated inoculations were necessary to obtain growths. These results were soon corroborated at the Leprosy Investigation Station of the United States Public Health and Marine Hospital Service at Honolulu, H. I.

Currie, Brinkerhoff, and Holman (*Public Health Reports*, 1910, xxv, No. 34) repeated Clegg's work on the cultivation of the leprosy bacillus and have also succeeded in obtaining growths of acid-fast organisms upon artificial media. These investigators pointed out additional factors which are not mentioned in Clegg's article and which are necessarty to insure successful results. The amœbæ must be active in order to obtain a pure symbiotic culture with the cholera vibrio. The agar slants must have a slight excess of condensation water, since the long period of incubation results in a considerable desiccation of the

media. Before adding the leprosy material to the amœba-cholera culture the workers at Honolulu found that it was desirable to keep the amœba-cholera culture at 37° C. for five days in order to encourage the encystment of the amœbæ. Under these conditions the amœba were found to be far less phagocytic, and this inhibition of phagocytosis appears to be essential in order to prevent the digestion of the leprosy bacilli. Along somewhat similar lines, but with slightly modified technique, Duval, of New Orleans also obtained an acid-fast bacillus in pure cultures from leprosy material.

Duval (*Jour. Exper. Med.*, 1910, xii, 649 to 665) cultivated an acid-fast bacillus by growing it in a symbiotic culture of the amœba and typhoid bacillus. The agar was alkaline to the extent of 1 per cent., and the amœba-typhoid culture was grown at room temperature for forty-eight hours before the introduction of the leprosy material. After the acid-fast organisms had grown the typhoid bacillus was killed by a strong bacteriolytic serum and it was found that under these conditions the leprosy bacillus grew in symbiosis with the amœbæ. It was not possible to obtain growths of the leprosy bacillus in symbiosis with the typhoid bacillus alone. The amœba appears to be the essential factor. Duval also tried a medium containing tryptophan, cystin, and leucin (1 per cent. of each). His idea was to supply food for the leprosy bacilli analogous to that of the tissues. He used this medium on the surface of banana slants in order to promote oxidation. Agar slants were similarly treated with these substances and the amœba-leprosy culture grew both on the banana slants and agar slants under these conditions. According to Duval the optimum temperature of growth for the leprosy bacillus in artificial media appears to be between 32° and 35° C., and the presence of light is an important feature. The organisms thus obtained grew in subcultures and were acid-fast. They were proved not to be tubercle bacilli by inoculation experiments in guinea-pigs and rabbits. Inoculation experiments were successful in Japanese dancing mice. The earliest macroscopic changes appeared after four weeks as discreet glistening nodules, $\frac{1}{2}$ mm. in diameter, and firmly attached to the serous surface of the peritoneal organs. Histological structures were the same as those in human lesions. Inoculations into the mice both with artificially cultivated organisms and from human cases of leprosy were successful, and it would appear that this successful direct inoculation helps to establish the identity of the organism in the artificial cultures. Duval's work differs in one respect materially from that of Clegg as well as Currie, Brinckerhoff, and Holman in that he found that his organisms grew best at 32° to 35° C., and that body temperature seriously inhibited or even prevented their growth. The other investigators, on the contrary, were always successful in obtaining growths at 37°. As the leprosy bacillus grows well in the human tissues, we would expect *a priori* that 37° C. would be its optimum temperature under conditions of artificial cultivation. The cultivation of the bacillus of leprosy has long been a stumbling block to the bacteriologist, but it now appears that we have at last the true solution of this crux. Of the hundreds of attempts to grow this organism in the past, that of Weil of the Pasteur Institute deserves special mention. He obtained one colony of an acid-fast organism upon rabbits' serum.

Chemo-immunological Studies on Localized Infections.—In spite of a large amount of experimental work upon pneumococcus infections it is not at all clear as to the manner in which the body protects itself against local infections of the pneumococcus. Antipneumococcus serum, it is known, has agglutinative properties, but no lytic action upon the pneumococcus. The serum, however, contains opsonins which further to a certain extent phagocytosis of pneumococci by leukocytes. Under ordinary circumstances the facility with which pneumococci are taken up by leukocytes varies greatly, the virulent strains being almost insusceptible of phagocytosis. LAMAR (*Journal of Experimental Medicine*, 1910, xiii, 1) has found that highly dilute solutions of alkaline oleates which do not suffice to alter the morphology or reproductive power of pneumococci, nevertheless produce profound changes in their structure; for pneumococci treated with sodium oleate not only become more subject to autolysis, but become subject to lysis by blood serum. The lysis is more marked when immune serum is used. It is necessary, however, that the sodium oleate should act upon the pneumococci in the test-tube before serum is added, since the serum protein contains a substance inhibiting the action of sodium oleate. It was found that boric acid in proper amount would prevent the inhibitive action of serum against sodium oleate. A mixture, therefore, of sodium oleate, boric acid, and serum was capable of killing pneumococci in vitro and preventing the infection of a susceptible animal from the injection of a lethal dose of pneumococci. And infection can not only be prevented when the mixture of immune serum, soap, and boric acid is added to the pneumococci before injection into the peritoneal cavity of small animals, but the infection can likewise be prevented when a therapeutic injection of a mixture of these three substances mentioned is made to follow the inoculation of highly virulent diplococci. Though the virulence of the pneumococci is somewhat diminished by soap treatment, the treated organisms are not rendered more susceptible to phagocytosis. It would appear that the action of soap is exerted upon the lipoidal moiety of the bacterial cells through which they are rendered more susceptible of destruction by serum. The experiments which have just been described represent a manner of disposing of pneumococci which in all probability takes place in a resolving pneumonic exudate, the autolyzing leukocytes furnishing the chemical substance which brings the pneumococci under the deleterious influence of body fluids.

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